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PART I

JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY

INTERNATIONAL RECORD OF CLINICAL AND RESEARCH PSYCHIATRY

The *Journal of Clinical and Experimental Psychopathology* was founded in 1939 by V. C. Branham, M.D., as the *Journal of Criminal Psychopathology*. In 1944 the title was changed to the *Journal of Clinical Psychopathology*; in 1951 the journal became the *Journal of Clinical and Experimental Psychopathology*. The present title (*Journal of Clinical and Experimental Psychopathology and Quarterly Review of Psychiatry and Neurology*) was assumed in 1954.

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Clinical Psychopathologic Conferences are often included as a feature of the JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY. This section will attempt to further the elucidation of correlations and associations between clinical, neurologic, psychologic, and biologic elements. Clinical case presentations illustrative of psychophysiopathologic disorders will be gathered from psychiatric hospitals, clinics, and psychiatrists throughout the world. Manuscripts together with accompanying illustrations should be forwarded to the JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY, 30 East 60th Street, New York, N. Y., Attention: Editor, Clinical Psychopathologic Conferences.

QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY

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PSYCHIATRY ABSTRACTS

Alcoholism and Drug Addiction

Clinical Psychiatry

Heredity, Eugenics, and Constitution

Psychiatry of Childhood

Psychiatry and General Medicine

Psychiatric Nursing, Social Work, and Mental Hygiene

Psychoanalysis

Treatment

A. General Psychiatric Therapy

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Studies of Ceruloplasmin in Schizophrenics and Normal Controls

*John C. Saunders, M.D., and Hisaac Chipkiewicz, M.S.**
ORANGEBURG, NEW YORK

Many studies were initiated following the report by Akerfeldt[1] that the sera of schizophrenic patients was capable of oxidizing N,N-dimethyl paraphenylene diamine dihydrochloride (DPP) at a greater initial rate than the sera of normal controls. This oxidation was attributed to ceruloplasmin, which is a copper globulin complex present in mammalian serum. Holmberg and Laurell[2–4] demonstrated that ceruloplasmin is a polyphenol oxidase capable of acting on a great variety of substrates. Ceruloplasmin is an α_2-globulin with a molecular weight of approximately 151,000 that contains 8 atoms of copper per molecule and accounts for over 95 per cent of the copper present in human plasma.

The difference between schizophrenic and normal individuals in rates of oxidation of DPP is illustrated by the slopes of the curves in figure 1. This difference may be due to the fact that either the concentration of ceruloplasmin is greater in the sera of schizophrenics or the concentration of a decelerant factor is greater in the sera of the normal controls. Scheinberg[5] reported a statistically significant difference in the concentration of ceruloplasmin when he compared normal with schizophrenic subjects using a direct spectrophotometric determination of this copper globulin complex.

The method used in the present investigation was developed by Chipkiewicz[6] and is comparable to that of Scheinberg.[5] It quantitates ceruloplasmin by following the rate of oxi-

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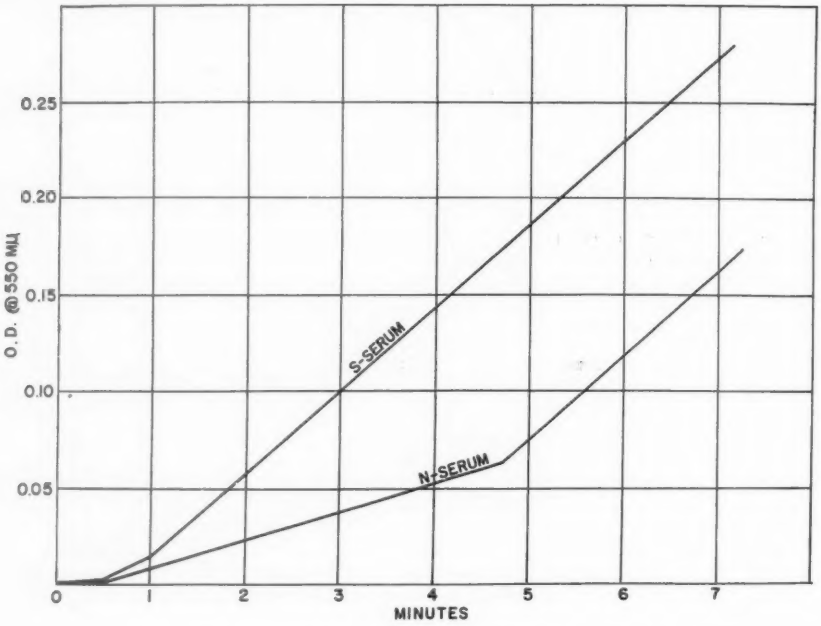

FIG. 1. Difference between schizophrenic and normal subjects in rates of oxidation of DPP.

dation of DPP. This study included 112 chronic schizophrenic men (hospitalized for three years or more) and 56 men of the hospital staff as normal controls. We found a statistically significant difference between the two groups (table I) but with an overlap of 63 per cent (fig. 2), which makes the rate of oxidation of DPP or the concentration of ceruloplasmin in serum insufficient as a criterion for diagnostic concepts. It is necessary to remember, however, that medical diagnosis is made with data obtained from several tests, since it is a multivariate, multidimensional problem of decision.

It was deemed necessary to measure the influence of ascorbic acid on the oxidation of DPP by serum because of previous reports[7] of the effect of this vitamin on this reaction, and because ascorbic acid oxidase is also a copper-protein complex.[8] Ascorbic acid was

TABLE I

Ceruloplasmin Concentration

	No. of patients	Average	Standard deviation	Difference
Controls (normal)	56	22.4	±3.0	3.5 ± 1.05 with 95% confidence
Schizophrenics	112	25.9	±3.5	

reported[7] to be the principal factor for the higher induction period found in normal controls because it was oxidized prior to the DPP; since the same induction period was not observed in all individuals with a clinical diagnosis of schizophrenia, it was concluded that they must have a lower concentration of ascorbate. We measured the levels of ascorbate using the method of Roe and Kuther[9] and its effect on the degree of oxidation of DPP during the initial five minutes. A sampling was taken from the original groups (8 from the normal and 12 from the schizophrenic) for base line values of ascorbic acid and degree of DPP oxidation after five minutes of incubation. These determinations were repeated on the fourth day after the oral daily administration of 500 mg. of vitamin C for three days. The serum ascorbic acid levels increased to approximately double the base line values; it was expected that this elevation would proportionally increase the induction period and therefore decrease the degree of DPP oxidation. The data did not support this concept, since we found no significant differences between the control and schizophrenic subjects in the base line levels of ascorbic acid; furthermore, after a twofold rise in ascorbate, there was no significant change in the induction period of either group. There were two exceptions where the base line ascorbic acid approached scurvy levels. (See table II.)

The outstanding chemical property of vitamin C is its reversible oxidation-reduction equilibrium between dehydroascorbic acid and ascorbic acid, respectively. Only the re-

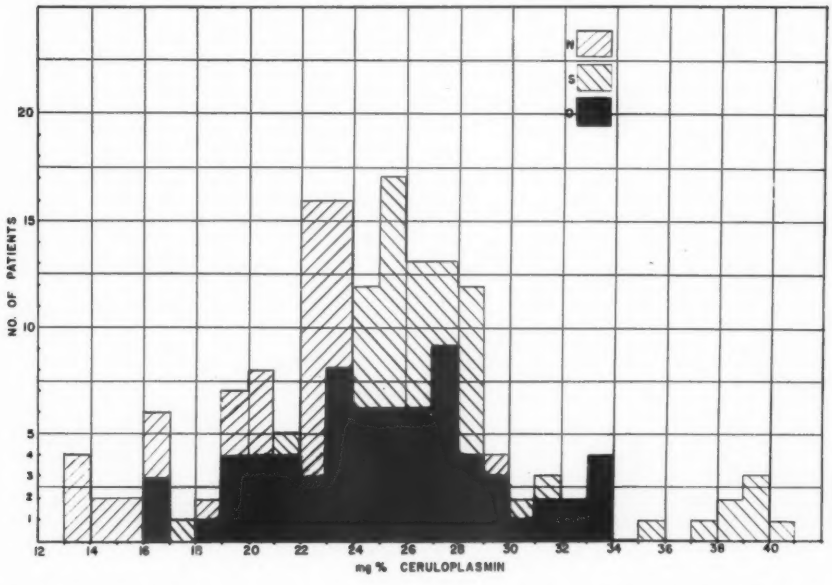

FIG. 2. Distribution of the concentration of ceruloplasmin in schizophrenics and normal subjects. Note 63 per cent overlap. N = normals, S = schizophrenics, and O = overlap.

TABLE II

*Effect of Administration of Ascorbic Acid on Oxidation of DPP**

	No. of patients	Before ascorbic acid		After ascorbic acid	
		Total ascorbate, mg. %	DPP oxidized	Total ascorbate, mg. %	DPP oxidized
Controls (normal)	8	0.76 (0.35–1.10)	24.5 (17.5–45.3)	1.42 (0.90–1.90)	24.3 (17.4–30.3)
Schizophrenics	12	0.66 (0.30–1.10)	29.3 (21.7–43.3)	1.28 (0.70–2.00)	29.1 (21.3–35.0)

* In $\mu M/5$ min./100 ml. of serum. The results presented are for total ascorbate, e.g., ascorbic, dehydroascorbic, and α-ketogulonic acid.

duced form (ascorbic acid) is capable of increasing the duration of the induction period in the oxidation of DPP by serum. Therefore, we measured both forms to determine whether there was any difference in the ratio of dehydroascorbic to ascorbic acids in the two groups. The same ratio was found to exist for both the normal and the schizophrenic subjects before and after the administration of ascorbic acid. The results of these experiments are shown in table III.

The results were interpreted as showing that ascorbic acid levels were only a minor factor in producing the induction period. The principal inhibitor of the enzymatic oxidation of DDP appears to be a nondialyzable factor (protein) and its inhibiting effect can be minimized by serial dilution.[10, 11] The mode of action of the inhibiting factor on the enzyme is probably through chelate formation,[12] since the primary effect of certain proteins in a biologically active molecule is to regulate the intensity and duration of the bonds for essential enzymatic processes. This would aid in explaining the relative stability and constant level of the copper complex in plasma.

TABLE III

*Mean Ratio of Ascorbic Acid to Dehydroascorbic Acid in Serum**

	No. of patients	Ascorbic acid administration	
		Before	After
Controls (normal)	6	0.81 (0.77–0.835)	0.80 (0.78–0.84)
Schizophrenics	6	0.80 (0.75–0.85)	0.80 (0.77–0.86)

* The reduced form (ascorbic acid) was determined by titration with 2,6-dichlorophenol indophenol, i.e., the fraction that is capable of reducing this dye and that could therefore reduce oxidized DPP.

TABLE IV

Oxidation Time in Seconds for One Micromole of Cysteine

	No. of patients	Mean and range	Standard deviation	Difference
Controls (normal)	10	1186 (1045–1380)	±21	164 ± 34 with 95% confidence
Schizophrenics	20	1021 (856–1225)	±55	

To characterize the induction period further, the following reaction was performed in a Thunberg tube with 1 ml. of 0.001 *M* cysteine freshly prepared, and 1 ml. of 0.01 *M* DPP buffered with 2.8 ml. of 0.05 *M* citrate at *p*H 5.5; in the upper chamber we added 0.2 ml. of fresh serum. After evacuation of the tubes, they were inverted, shaken vigorously, and incubated at 37 C. The reaction was timed in seconds until its end point was determined by the appearance of a pink color from the oxidized DPP. This point was easily detectable, since the color becomes a bright pink 10 seconds after the initial color change. The development of color indicates the complete oxidation of the cysteine present, the reaction sequence being as follows:

$$(1) \qquad 2\ \text{DPP (red.)} \xrightarrow[\text{Ceruloplasmin}]{(O)} 2\ \text{DPP (oxid.)}$$

$$(2) \qquad 2\ \text{DPP (oxid.)} + 2\ \text{Cysteine} \longrightarrow 2\ \text{DPP (red.)} + \text{Cystine}$$

$$(3) \qquad (1) + (2) \qquad 2\ \text{Cysteine} \longrightarrow \text{Cystine}$$

The results of this experiment are presented in table IV.

The statistical interpretation of the data presented in table IV indicates that the difference between schizophrenic and normal control subjects was highly significant at the 95 per cent confidence level. The results obtained could be explained in terms of ceruloplasmin concentration and also as a result of more inhibitor in the normal control serum. This study indicates the possibility of a diagnostic test, although further elucidation of the reaction must be made for this purpose. We are now applying this test widely in order to determine its usefulness.

SUMMARY AND CONCLUSIONS

The concentration of ceruloplasmin in the sera of schizophrenic subjects was found to be significantly increased when compared to that of normal control subjects. This difference is not applicable to differential diagnosis because of an overlap of 63 per cent between the two groups. It was observed, also, that ascorbic acid was not the exclusive factor for the increased induction period of the DPP oxidation rate in the normal controls. Preliminary

dilution experiments indicate that the principal inhibiting factor was present at higher levels in the sera of normal controls than of schizophrenic subjects. We are continuing our studies of the induction period in order to elucidate the possible mechanism of this phenomenon with the probability that it will provide added insight into the etiology of schizophrenia. The experiments in the oxidation of cysteine to cystine presented a highly significant difference in the rates of oxidation between normal control and schizophrenic subjects. This difference was found to be 164 ± 34 seconds with a 95 per cent confidence level. The oxidation of cysteine will be evaluated in other clinical entities in order to define its possible usefulness as a diagnostic aid for schizophrenia. There are several theoretical implications in regard to sulfhydryl metabolism that may coincide with processes of this psychosis.

ACKNOWLEDGMENTS

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RESUMEN

La concentración de ceruloplasmina en el suero de esquizofrénicos, se halló significativamente aumentada cuando se comparó con la de sujetos normales testigos. Esta diferencia no es aplicable al diagnóstico diferencial en virtud de una imbricación del 63 por ciento entre los dos grupos. Se observó también que el ácido ascórbico no fue el único factor que produjo el aumento del período inductivo para la oxidación dicloridrato de N,N-dimetilparafenilendiamina en los testigos normales. Los experimentos preliminares de dilución indicaron que el factor inhibitorio principal se hallaba presente a concentraciones más elevadas en el suero de los testigos normales que en el de los esquizofrénicos. Continuamos nuestros estudios sobre el período de indución para elucidar el posible mecanismo de este fenómeno con la probabilidad de que proporcione nueva luz sobre la etiología de la esquizofrenia. Los experimentos sobre la oxidación de la cisteína a cistina, revelaron que existe una importante diferencia entre las velocidades de oxidación correspondientes a testigos normales y a esquizofrénicos. Esta diferencia era de 164 ± 34 segundos, con un margen de precisión del 95 por ciento. Se evaluará la oxidación de la cisteína en otras afecciones clínicas para establecer su posible utilidad en el diagnóstico de la esquizofrenia. Hay varias implicaciones teóricas en relación con el metabolismo del sulfhidrilo que pueden correlacionarse con los procesos existentes en esta psicosis.

RESUME

La concentration de céruloplasmine dans le sérum des schizophrènes a été trouvée augmentée de façon significative par rapport à celle des sujets-témoins normaux. Cette différence n'est pas applicable au diagnostic différentiel, à cause d'un chevauchement de 63% entre les deux groupes. Il a été également observé que l'acide ascorbique n'était pas le facteur exclusif responsable de l'augmentation de la période d'induction du taux d'oxydation

de dichlorydrate de N,N-dimethyl paraphénylène diamine chez les sujets-témoins normaux. Les épreuves de dilution préliminaires indiquent que le facteur principal d'inhibition était présent à concentration plus élevée dans le sérum des sujets-témoins normaux que chez les schizophrènes. Les auteurs poursuivent les études sur la période d'induction dans le but d'élucider le mécanisme possible de ce phénomène en présumant que cette information ajouterait à nos aperçus sur l'étiologie de la schizophrénie. Les expériences sur l'oxydation de la cystéine en cystine ont révélé un écart hautement significatif dans les taux d'oxydation entre les sujets-témoins normaux et les schizophrènes. L'écart trouvé était de 164 ± 34 avec un niveau présumé de 95%. L'oxydation de la cystéine sera évaluée dans d'autres entités cliniques de manière à déterminer son utilité éventuelle comme moyen de diagnostic de la schizophrénie. Il existe plusieurs implications théoriques à l'égard du métabolisme sulfhydryle pouvant coïncider avec les processus de cette psychose.

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Azacyclonol: Studies in Selection of Patients, Dosage, and Administration

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On February 11, 1955, Fabing described the effect of azacyclonol (Frenquel*) upon certain psychic manifestations of LSD-25 poisoning in human beings,[1] and he proposed that the drug might be useful in certain spontaneous and toxic psychoses. The literature published since that time contains several contradictory reports, but four independent double blind studies have been conducted that indicate that hallucinations and delusions frequently (but not invariably) respond favorably to azacyclonol therapy. Rinaldi et al treated a series of 39 chronically ill, psychotic patients, using a daily dose of 20 mg. of azacyclonol by mouth,[2] and, at a later date, repeated this study in the same patients, using 400 mg. daily.[3] Mason-Browne reported a study of 64 psychotic woman patients in which he employed azacyclonol in a dose of 60 mg. daily by mouth.[4] Odland in a study involving 171 chronic schizophrenic patients,[5] and Coats, Gray, and MacQuiddy in their series of 131 elderly psychotic patients,[6] used azacyclonol in a dose of 100 mg. daily by mouth. All these studies not only confirm Fabing and Hawkins' observation that many psychotic patients are benefited,[7] but they also call attention to the disturbing fact that many patients with hallucinations or delusions are not helped. The difficulty in properly evaluating any new drug that influences psychotic behavior is enhanced by the use of concurrent therapy. This is perhaps best illustrated by the following case summary kindly provided by Bowers:[8]

> A patient in hostile transference, who did not wish either to ask me for the Frenquel or to spend money on buying it, stole some of it from my quarters. Being unused to drug labels she picked up a bottle of placebo which had been opened and helped herself. She had been on Frenquel for four months, and my associate with whom she is in current treatment had maintained that her improvement during this period was at last the reward of our more than five years of patient therapy. Suddenly, she was as sick as ever. Out of contact with reality in general, living in a dream world with a flight of ideas, in general the picture we have had to contend with for many years. This patient has had therapy for about 10 years, and two hospitalizations. In trying to find out what had caused her sudden and unexplained regression, he stumbled on the story of her theft of the Frenquel. He then asked to see the tablets, tasted them and realized that she had been on placebo throughout the entire period of pronounced regression. She then asked me for more Frenquel, and within a very few days was operating at the level of her previously improved functioning. This experience convinced my associate that the Frenquel had been the precious ingredient of the progress she had made since July.

The difficulty in the selection of patients for therapy with any one or any combination of the psychopharmacologic agents probably results from our inability to understand the various metabolic defects or abnormalities that produce the symptoms associated with serious nervous and mental disease. Since there is probably a variety of unknown but suspected metabolic defects,[9] it is reasonable to expect that a drug that corrects one type of

From Traverse City State Hospital, Traverse City, Mich.

* The trade name of The Wm. S. Merrell Company, Cincinnati 15, Ohio, for azacyclonol is Frenquel.

defect will be effective only in those psychotic patients suffering from that particular enzymatic or metabolic abnormality. Until the physical pathogenesis of mental symptoms is as well understood as the bacteriologic pathogenesis of the infectious diseases, selection of patients for specific drug therapy will continue to be on a purely empirical basis. A satisfactory procedure for such selection has been developed in the case of azacyclonol.

SELECTION OF PATIENTS FOR AZACYCLONOL THERAPY IN THE HOSPITAL

Before azacyclonol is administered orally, three doses of 100 mg. each should be given intravenously at intervals of four hours. It is preferable to do this for three consecutive days, but those patients who ultimately will benefit from oral azacyclonol therapy usually show some change in delusions or hallucinations during the first day. The nature of the change is important. Azacyclonol is not an immobilizing agent that can be expected to sedate virtually all overactive patients.[10] In those patients who have been overactive or assaultive as a result of delusional activity, azacyclonol may appear to have tranquilizing or sedative properties as the behavior becomes relatively more normal as a response to the decrease in intensity of the delusions or hallucinations. From a therapeutic point of view, it is, of course, essential that the patient become completely free from hallucinations and delusions, but from the testing point of view partial improvement following the series of intravenous test doses is adequate. For example, a patient who believes that she is the Queen of England may still have delusions following intravenous azacyclonol. However, if she now believes she is a less important queen of a minor country, this change would be regarded as sufficiently encouraging to justify long-term therapy with oral azacyclonol.

SELECTION OF PATIENTS IN OFFICE PRACTICE

Many disturbed patients are seen on an ambulatory basis, not only by specialists but also by general practitioners. The intravenous test outlined above may be inconvenient since it involves three injections a day, preferably for three days, and a considerable amount of personal observation. It is suggested that a useful alternative procedure would involve a single intravenous injection of 100 mg. of azacyclonol, preferably on each of three days rather than in a single day, supplemented by 200 mg. of oral azacyclonol daily during the test period. Any favorable change in behavior during the test period should be interpreted as an indication for continued azacyclonol therapy that can be administered orally.

SELECTION OF CHILDREN FOR AZACYCLONOL THERAPY

In children there is sometimes a problem of differential diagnosis, since childhood schizophrenia resembles mental deficiency in many cases. Azacyclonol is not usually helpful in overactive, mentally deficient patients,[11] but it is extremely useful in childhood schizophrenia. Bender and Nichtern[12] reported the successful use of azacyclonol in children, using a daily oral dose of 1 mg./lb. of body weight. It is suggested, therefore, that children for whom there may be a question of the differential diagnosis between mental deficiency and schizophrenia should be treated with azacyclonol in a daily dose of 1 mg./lb. of body weight a day for a period of four weeks. Those who do not respond are likely to be mentally

deficient, and no further azacyclonol would be indicated. Those in whom behavior is improved should continue to receive azacyclonol along with other psychopharmacologic agents indicated for relief of specific manifestations of psychotic behavior.

ORAL MAINTENANCE DOSAGE OF AZACYCLONOL

The daily oral dose of azacyclonol described in the literature varies from 20 mg.[2] to 1200 mg.[10] Since the response to azacyclonol appears to be a qualitative rather than a quantitative phenomenon, the relatively small doses are as satisfactory as large ones. At the Traverse City State Hospital, an attempt was made to determine the practical minimum for daily maintenance therapy. A group of 164 women patients, selected because of their favorable response to intravenous azacyclonol, was subjected to several different dosage schedules. The most satisfactory response was obtained when 40 mg. three times daily was given. However, this involved distribution of medication three times daily to each patient. Accordingly, all patients were switched to a single oral dose of 100 mg. Those patients who did not respond as well to the single doses were then given 100 mg. twice daily, and if the dose still was not adequate it was increased to 100 mg. three times daily. At the end of a 14 week test period, 76 of a total of 164 patients were adequately maintained on 100 mg. once daily by mouth, 65 required 100 mg. twice daily, and only 23 needed 100 mg. three times daily.

SUMMARY AND CONCLUSIONS

Azacyclonol is effective in the treatment of some psychotic patients but not of others. Accordingly, the selection of adult patients likely to benefit from oral azacyclonol therapy is facilitated greatly by a short test course of the drug administered intravenously; the selection of children for such therapy depends upon their response to a longer test course of oral azacyclonol. Those who respond at least partially to azacyclonol during the test period should then be orally treated with azacyclonol. In adults, the maintenance dose may be 40 mg. three times daily or 100 mg. given one to three times daily. In children, the daily oral maintenance dose is 1 mg./lb. of body weight. When azacyclonol is given orally to patients who have previously responded to the test doses, favorable therapeutic results may be expected in the majority of patients.

RESUMEN

El azaciclonol es eficaz en el tratamiento de algunos pacientes psicóticos, pero no en otros. Por consiguiente, la selección de los enfermos adultos que podrían beneficiarse con la terapia con azaciclonol por vía oral, se facilita muchísimo por medio de un corto tratamiento de prueba, con la droga administrada por vía intravenosa. La selección de los niños para tal terapia depende de su respuesta a un tratamiento de prueba más prolongado, por vía oral, con azaciclonol. Los que responden al azaciclonol durante el período de prueba, aunque sea parcialmente, deben ser tratados por vía oral con este medicamento. En los adultos la dosis de mantenimiento puede ser de 40 mg. tres veces al día o de 100 mg. administrados una a tres veces diarias. En los niños, la dosis diaria de mantenimiento es de

2 mg./Kg. de peso corporal. Cuando se administra azaciclonol por vía oral a pacientes que respondieron previamente a las dosis de prueba, se pueden esperar resultados terapéuticos favorables en la mayoría de ellos.

RESUME

L'azacyclonol est efficace dans le traitement de certains malades psychotiques, mais pas chez d'autres. En conséquence, la sélection des malades adultes aptes à bénéficier d'un traitement oral par l'azacyclonol est grandement facilitée par un court traitement d'épreuve par voie intraveineuse. La sélection des enfants aptes à bénéficier de cette médication dépend de la réponse à un traitement d'épreuve plus prolongé par l'azacyclonol par voie orale. Ceux qui répondent, au moins partiellement, à l'azacyclonol durant le traitement d'épreuve doivent alors être traités par l'azacyclonol oral. Chez l'adulte, la dose d'entretien peut être de 40 mg. trois fois par jour ou de 100 mg. administrés une à trois fois par jour. Chez l'enfant, la dose d'entretien quotidienne d'azacyclonol par voie orale est de 1 mg./450 g. de poids corporel. Quand l'azacyclonol est donné par voie buccale au patient ayant précédemment répondu aux doses d'épreuve, on peut s'attendre à obtenir de bons résultats thérapeutiques chez la plupart d'entre eux.

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Mepazine in the Treatment of Psychiatric Disorders with One Year Follow-up

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Investigations both here and abroad have established the value of mepazine* in the treatment of various psychiatric disorders, particularly those of the schizophrenic type.[1–5] In this present study, it was our plan to determine whether or not hospitalized patients who have improved on mepazine therapy maintain this improvement over long periods of time. Therefore, after a thorough study of mepazine in 125 patients with various mental illnesses, a follow-up of the largest diagnostic group was made one year after completion of the original study.

CLINICAL MATERIAL

For a period of three months the majority of newly admitted psychotic patients on the male service of the Central State Hospital at Nashville, Tenn., were routinely placed on mepazine. These patients were predominantly schizophrenics. Other patients treated in this study included chronically disturbed individuals with long hospitalization and patients who showed no lasting effect from previous treatment with electroconvulsive therapy, chlorpromazine, promazine, or other agents. This total of 125 patients was on mepazine therapy for periods ranging from one to six months. Table I shows the number of patients in each diagnostic category.

ADMINISTRATION

Initially the patients were started on 50 or 100 mg. of mepazine daily, administered orally or intramuscularly. Increments of 50 mg. were added daily. It was soon observed that this rapid build-up of the dosage was not beneficial for the patients and, moreover, seemed to be the main cause for the occurrence of certain side effects. Therefore, smaller increments (25 mg.) were administered every five to seven days. After a sufficient adaptation on a lower dosage, the patients tolerated the following increments well. Only in acute cases when severe disturbances had to be dealt with and the patients were in good physical health were larger increments utilized at somewhat shorter intervals.

The average optimal dosage of mepazine was 300 mg./day. When a satisfactory response was obtained and maintained for a week, the dosage was, in similar manner, gradually decreased and adjusted to the needs of the patient. The average maintenance dose was 100 mg./day.

From Central State Hospital, Nashville, Tenn.

* The trade name of Warner-Chilcott Laboratories for mepazine is Pacatal. The mepazine used in this study was supplied by Warner-Chilcott Laboratories.

TABLE I

Diagnostic Categories

Type of illness	No. of patients
Schizophrenic reactions	67
Convulsive disorders	16
Chronic brain syndrome	10
Mental deficiency	8
Alcoholism	7
Manic depressive psychosis	5
Other	4
Psychosis (undetermined type)	3
Neurosis	2
Involutional psychotic reaction	2
C. N. S. syphilis	1
Total	125

CRITERIA FOR IMPROVEMENT

The clinical terms used to describe the degree of improvement were as follows: Slight improvement meant subsidence of acute symptoms with greater manageability on the ward. Moderate improvement meant a fair to good adjustment within the hospital with participation in group activities. Excellent improvement indicated that the patient was ready for home visits or discharge.

RESULTS

The effect of mepazine was usually more calming than hypnotic. The patients were less detached and withdrawn. They were not apathetic or emotionally blunt as is so frequently observed with other ataraxics. Patients were tranquil, alert, and had good contact with their surroundings. They also became more accessible for psychotherapy and integrated more easily into the group. Their better cooperation in ward activities was in turn reflected in the morale of the nursing personnel.

Our results showed that the degree of improvement in the schizophrenic patients, irrespective of the particular type of schizophrenic classification, was related to the length of illness and hospitalization. An analysis of these data appears in table II. A few patients classified as slightly improved in the study improved further on additional treatment with mepazine after the study had been completed. The excellent improvement obtained by 1 patient in group 3 deserves special mention.

Case 1. E. J., a man aged 26, had been overtly sick for nine years and was treated in nine different hospitals for a total period of two years and six months. He had received electroconvulsive therapy, insulin, and chlorpromazine with no lasting results in any of these hospitals. He was a behavior problem with a history of constant outbursts of violence and hostility and escapes from previous hospitals. Mepazine administration en-

TABLE II

Effectiveness of Mepazine in Schizophrenic Patients

Group	No. of pt.	Hospitalized, yr.	Duration of illness, yr.	Improvement			
				Exc.	Mod.	Slight	None
1	8	Up to ½	Up to 1	2 (25%)	2 (25%)	3 (38%)	1 (13%)
2	14	Up to 1	2–8	5 (36%)	7 (50%)	2 (14%)	0 (0%)
3	13	1–5	3–16	2 (15%)	4 (31%)	6 (46%)	1 (8%)
4	15	5–10	7–25	0 (0%)	3 (20%)	7 (47%)	5 (33%)
5	17	10+	10–39	0 (0%)	2 (12%)	7 (41%)	8 (43%)
Total	67			9 (13%)	18 (27%)	25 (37%)	15 (22%)

abled him to participate in the recreation program and work in the dining room at Central State Hospital. While at this hospital he never caused any serious trouble and is being granted a trial visit home. He has been on mepazine for more than two months, receiving up to 600 mg. daily. Except for a slight temporary blurring of vision he has had no side effects.

Another interesting development in the course of our study was the finding that a patient in group 4 who showed only a slight improvement after a three month course of mepazine became accessible to psychotherapy for the first time in seven and one-half years of hospitalization after mepazine discontinuance.

Table III shows the results of mepazine therapy in treating patients with manic depression, involutional psychoses, psychoses of undetermined type, neuroses, alcoholism, convulsive disorders, mental deficiency, chronic brain syndromes, syphilis of the central nervous system, and miscellaneous disturbances.

Sixteen patients with convulsive disorders (2 of them with Little's disease) were treated with mepazine because of psychotic symptoms. One particularly interesting case follows.

Case 2. T. B. S., aged 38, is a man whose diagnosis was chronic brain syndrome with convulsive disorder. Ill since the age of 8, he had been hospitalized continuously for the past seven and one-half years. He had been on anticonvulsants and phenobarbital for many years. Numerous episodes of psychotic behavior, violence, and aggression had occurred, and he was regarded as one of the most dangerous patients on the male service. Electroconvulsive therapy and a variety of ataraxics and sedatives had been tried in an effort to ease this desperate patient management problem. Phenobarbital was given to the point of toxicity.

He was one of the first patients to be treated with mepazine. The initial response was surprisingly good and rapid (after only one week). He received up to 500 mg. daily for the first few weeks and has been adequately maintained for several months on 300 mg. daily; phenobarbital was discontinued without any change in the pattern of occurrence of convulsions. Now he is more alert, interested in his surroundings, and cooperative in ward activities. Hostility has subsided, and overt psychotic symptoms have been absent for about five months.

SIDE EFFECTS

In our series of 125 patients, side effects occurred in 67 patients, or 54 per cent, that were more annoying than serious. Among the side effects observed, of which more than one may

TABLE III

Effectiveness of Mepazine in Nonschizophrenic Patients

Diagnosis	No. of pt.	Results			
		Slight	Mod.	Exc.	None
Manic depression					
Manic	1	—	1	—	—
Cyclic	1	—	1	—	—
Depression	3	—	—	2	1
Involutional psychosis	2	—	2	—	—
Psychoses, undetermined type	3	—	2	1	—
Neuroses	2	1	—	1	—
Alcoholism					
With psychosis (D.T.)	4	1	—	3	—
Without psychosis	3	1	1	—	1
Totals	19	3	7	7	2
Convulsive disorders					
Little's disease	2	—	2	—	—
Others	14	5	4	1	4
Mental deficiency	8	4	2	1	1
Chronic brain syndrome					
Presenile	1	—	—	—	1
Senile	1	1	—	—	—
Arteriosclerotic	8	—	3	2	3
C. N. S. syphilis	1	—	1	—	—
Miscellaneous	4	2	1	1	—
Totals	39	12	13	5	9

have appeared in the same patient, were dry mouth and sore throat, blurred vision, constipation, and slight drowsiness. Most of the side effects are due to its atropine-like effect and can be avoided or greatly minimized by careful adjustment of the dosage and/or by the use of adjunctive medication, such as neostigmine and laxatives. In 9 patients mepazine was discontinued because of a combination of fever, sore throat, and blurred vision (4 patients), convulsions (3 patients), and dermatitis (2 patients).

Although 2 patients developed dermatitis, 2 other patients with skin disorders improved on mepazine therapy. One of these patients, a 28 year old white man with the diagnosis of chronic brain syndrome with convulsive disorder since the age of 18 months, had suffered since adolescence from severe acne vulgaris, which failed to yield to numerous therapeutic efforts with a variety of topical agents. This patient showed an unexpected cure, so far lasting for more than 2 years, when mepazine, up to 150 mg. daily, was instituted. Three attempts to withdraw the drug resulted in prompt relapses within a few days. He is now maintained satisfactorily on 25 mg. of mepazine twice a day. It has been hypothesized that the neurogenic depression of nervous impulses to the sebaceous glands might be re-

sponsible for this improvement.* The other patient, a schizophrenic with a chronic neurodermatitis of 15 years' duration, showed some improvement for the first time.

As with other phenothiazine derivatives, convulsions may occur. One patient with a previous history of convulsions developed a seizure after 51 days of mepazine medication when his daily dose was reduced from 300 to 150 mg. Although the drug was discontinued immediately, one more convulsion followed. Another, an amateur boxer, on a daily intake of 100 mg. had two seizures within three weeks. Still another patient, diagnosed as having dementia praecox, developed status epilepticus 35 days after mepazine had been instituted in doses up to 400 mg. daily. In these 3 patients, convulsions ceased after the drug was withdrawn.

Other investigators have reported that mepazine is capable of lowering the threshold of cerebral discharge in cases with abnormal electroencephalographic patterns even if convulsive disorders have not been observed clinically. The known epileptics in this series showed no alteration of pattern or frequency of convulsions, as long as they were maintained on anticonvulsive medication while being treated with mepazine. Therefore, the concomitant use of anticonvulsants is essential in the treatment of all epileptics.

Mepazine, like all phenothiazine derivatives, may cause agranulocytosis. One case occurred after the original study was completed, and, although the patient had also been on chlorpromazine before mepazine was instituted, it is our belief that the agranulocytosis was related to the mepazine therapy. A description of the case follows.

A 61 year old, poorly nourished white man had been taking chlorpromazine as an outpatient for several months with little or no apparent effect. He was admitted to the hospital on February 21, 1957, with a diagnosis of agitated depression due to involutional psychosis, and was started on mepazine. The dosage was gradually increased to 200 mg. daily; he received a total of 4725 mg. during the next 46 days. On the forty-sixth day he complained of sore throat, and all oral medication was stopped. During the next few days he displayed a temperature ranging to 103.6 F., a mild icteric tint of the sclerae and skin, and his white blood count, which had been 7500 on admission, dropped to 3300. He was transferred to another hospital on the fifty-third day. Here he was noted to have an extensive exudative membrane covering the entire oral mucosa; the posterior pharynx was fiery red and hemorrhagic. The liver was enlarged, temperature persisted, and a second examination revealed a white blood count of 750 with 100 per cent lymphocytes. His condition rapidly became worse, and he expired on the fifty-sixth day of hospitalization.

DISCUSSION

As was to be expected and as has been noted with many other ataraxics, the chronic and deteriorated patients showed the least response to mepazine. Our findings tend to support the previously reported data that no one drug produces maximum benefit in every patient. However, an over-all improvement of 79 per cent with mepazine in 125 mentally ill patients with poor prognosis is impressive and should, we believe, encourage further studies. A large number of these patients had had long hospitalizations and showed no lasting benefits

* A recent study concerning the effect of chlorpromazine and mepazine on palmar sweat measures indicates a significant reduction of sweat gland activity in patients treated with mepazine during a period of 30 days.[7] It may follow that mepazine has a similar depressant effect on the innervation of the sebaceous glands.

TABLE IV

Discharge Rate of Schizophrenic Patients Related to Duration of Illness

Group	No. of pt.	Hospitalized, yr.	Duration of illness, yr.	Discharged from hospital	Returned to hospital
1	8	Up to ½	Up to 1	8	1
2	14	Up to 1	2–8	11	3
3	13	1–5	3–16	3	2
4	15	5–10	7–25	1	0
5	17	10+	10–39	0	0
Total	67			23 (34%)	6 (9%)

from other treatments. Individualized dosage adjustment was found to contribute greatly to the reduction of undesirable side effects. This is particularly true in chronic mental disorders where prolonged medication is necessary. Thus it should be mandatory to administer the drug under close clinical supervision.

In a few cases, where mepazine or chlorpromazine alone failed therapeutically, their combination proved to be more effective, with a significant reduction or elimination of side effects. Further investigation of this phenomenon is merited.

Since most of the patients who could be discharged were seen on their routine return visits to the outpatient department, we had the rare opportunity of being able to observe and follow up the drug's effectiveness after a full year (March, 1957, to February, 1958) in 67 schizophrenic patients.

Previously we had noted a certain relation between the duration of illness and length of hospitalization and the degree and incidence of improvement.

Of the group of 67 schizophrenics (see table IV), 23 (34 per cent) left the hospital in the course of one year, 2 of them against medical advice. Seventeen (74 per cent) of the 23 have so far remained on the outside. Six returned to the hospital because of a recurrence of their illness. Two of these 6 have since improved, and discharge is being considered in the near future. One of the 2 is again responding very well to mepazine, and the other is being treated with prochlorperazine.

We feel it is remarkable that, out of the group of 8 patients who were hospitalized up to one-half year and ill up to one year at the time the study was initiated, all left the hospital and only 1 returned for further treatment.

Of the second group of 14 patients hospitalized for up to one year but sick for two to eight years, 11 left the hospital and only 3 returned.

Of the group of 13 patients hospitalized for one to five years, but ill 3 to 16 years, 3 left the hospital, 2 returned, and 1, who was discharged against medical advice, did not return.

One patient out of the fourth group, with 5 to 10 years of hospitalization and 7 to 25 years' illness, improved on several more months of treatment with mepazine to such an extent that he could be discharged to his fortunately understanding family. He is now

being maintained on 100 mg. daily, is gainfully employed, and is seen regularly as an outpatient. In the original study this patient was rated as only slightly improved.

SUMMARY

One hundred and twenty-five institutionalized mentally ill patients were treated with mepazine in doses ranging from 150 mg. to 600 mg. daily for a period of one to six months. These patients included 67 schizophrenics, 16 with convulsive disorders, 10 with chronic brain syndrome, 8 with mental deficiency, 7 chronic alcoholics, and 17 others with miscellaneous psychiatric disorders. Excellent, moderate, or slight improvement was noted in 99 or 79 per cent of the 125 patients. Many of these had previously been shown to be resistant to various treatments. In a one year follow-up of 67 schizophrenic patients treated with mepazine, 23 (34 per cent) of this group left the hospital and 17 (27 per cent) have been at home for at least a year. Only 6 patients had to return for further treatment. In schizophrenia, the duration of the disease appears to be a determining factor in effective treatment. Patients ill for longer periods show less effective response to medication. Mepazine appears to be an effective drug in the treatment of many psychiatric disorders. It is a potent drug and not without certain side reactions. It should therefore be used under constant medical supervision.

RESUMEN

Se trataron con mepazina en dosis que oscilaron entre 150 a 600 mg. diarios, por un período de 1 a 6 meses, 125 pacientes mentalmente enfermos hospitalizados. Estos pacientes incluían 67 esquizofrénicos, 16 con trastornos convulsivos, 10 con síndrome cerebral crónico, 8 con deficiencia mental, 7 alcohólicos crónicos y 17 con trastornos psiquiátricos diversos. Se observó mejoría excelente, moderada o ligera en 99 (79 por ciento) de los 125 pacientes. Muchos de ellos habían mostrado previamente resistencia a varios tratamientos. De 67 pacientes esquizofrénicos tratados con mepazina y observados durante un año, 23 (34 por ciento) salieron del hospital y 18 (27 por ciento) estuvieron en casa durante un año, por lo menos. Sólo 6 pacientes tuvieron que volver al hospital para ser tratados de nuevo. En la esquizofrenia, la duración de la enfermedad parece ser un factor determinante de la eficacia del tratamiento. Los pacientes enfermos por más largos períodos de tiempo, responden menos eficazmente a la medicación. La mepazina parece ser una droga eficaz en el tratamiento de numerosos trastornos psiquiátricos. Es una droga potente con ciertas reacciones secundarias. Por lo tanto, debe emplearse bajo constante vigilancia médica.

RESUME

Cent vingt-cinq malades mentaux internés ont été traités par la mépazine à doses variant entre 150 et 600 mg par jour, pendant une période de un à six mois. Ce groupe comprenait 67 schizophrènes, 16 d'entre eux avaient des crises convulsives, 10 un syndrome cérébral chronique, 8 étaient des déficients mentaux et 7 des alcooliques chroniques, les 17 autres atteints de psychoses diverses. Une amélioration excellente, modérée ou légère a été ob-

servée chez 99 (79%) des 125 malades. Parmi ceux-ci, il y en avait beaucoup qui s'étaient montrés réfractaires à divers traitements antérieurs. Au cours d'une période d'observation d'une année portant sur 67 schizophrènes traités par la mépazine, 23 (34%) malades de ce groupe ont quitté l'hôpital et 18 (27%) sont rentrés à leur foyer depuis un an au moins. Il n'y a eu que 6 malades qui ont dû revenir pour poursuivre le traitement. Dans la schizophrénie, la durée de la maladie paraît être un facteur déterminant dans l'efficacité du traitement. Les malades atteints depuis longtemps sont ceux qui répondent le moins bien au traitement. La mépazine paraît être une drogue efficace dans le traitement de nombreuses psychoses. C'est un composé trés actif non dénué de certains effets secondaires. Son administration réclame donc une surveillance médicale constante.

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Tax Decision Affects Training of Internists and General Practitioners in Psychotherapy

The United States Tax Court has announced a decision that could encourage more internists and general practitioners to undertake study of psychiatric techniques. The tax court overturned an Internal Revenue Service ruling that expenditures for training in psychotherapy do not constitute a deductible business expense. The tax court held, in effect, that it is reasonable for a "general" physician to improve his value to patients by learning to recognize their emotional problems. Dr. John S. Watson of Worthington, Ohio, had listed as a business expense the $8900 he spent in fees, travel, and other charges over a two year period for a special course. When this was disallowed by the Internal Revenue Service, he was billed for $2500 in deficiencies. The tax court's overruling of the service should prove an economic incentive not only to training in psychiatric methods but to postgraduate education generally.

The Use of Fish in the Evaluation of Drugs Affecting the Central Nervous System

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Fish have been found suitable for the study and even the bioassay of drugs that affect the central nervous system.[1–3] In some particulars, there are advantages in using fish rather than mammals, for instance in the following: (1) Fish have highly coordinated reflex and motor systems that are necessitated by their existence in three instead of two dimensions; (2) their gills are semipermeable membranes through which many drugs can penetrate, and larger species can be injected with compounds that are not soluble or readily transported into the body via the gills; (3) they can respond to various stimuli by changes in color; (4) differences in behavior of closely related species can be utilized; and (5) they are relatively inexpensive and easy to maintain.

Modifications of behavior in different species of fish have been noted for a variety of drugs. Perhaps the best-known example is the apparent docility of the Siamese fighting fish (*Betta splendens*)[4, 5] after the administration of ataraxics such as chlorpromazine. Air snappers (*Macropodus operchlaris*) have been similarly used.[6]

We have used fish to study the action of various drugs on the central nervous system. The species investigated included the guppy (*Lebistes reticulatus*), the Mexican blind cave fish (*Anoptichthys hubbsi*), and the common goldfish (*Carassius auratus*). Each of these may show a characteristic behavior in the presence of certain drugs. The action and efficacy of the drugs were evaluated by initial observations of the fish and then of their responses when challenged with a stress situation, both under ordinary conditions and in the presence of drugs. Changes in physical appearance or modification in behavioral pattern were the factors considered in the evaluation of the drugs.

METHODS

Administration of Compounds. Agents were tested at dosage levels varying from the ineffective to the toxic by intraperitoneal injection; the vehicles were water, physiological salt solution, or 0.3 per cent carboxymethyl cellulose; the volume of injection was usually 0.05 ml. Compounds were also tested for gill permeability by permitting fish to swim in solutions of the material. When effects were obtained by administration through the gills, administration by injection was not always done.

General Observation. Fish were observed in an aquarium for normal appearance, swimming ability, and behavior. The same observations were then continued after the administration of drugs. A number of drugs produced convulsions in toxic concentrations; differences between excitement and depression were easily seen. In addition, the changes in skin

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color sometimes exhibited by guppies were noted.[7] Normally the color is adjusted to that of the background by chromophore stellation and contraction, but in the presence of certain drugs, including lysergic acid diethylamide, this reaction is altered and fish may darken even in a light background.

It was also possible to observe the response of the fish to visual and tactile stimuli. The operator's hand was placed in the aquarium and an attempt made to catch the fish, first by rapid and then by slow pursuit. Normal control fish always escaped, but under the influence of certain of the agents, especially ataraxics, the fish could easily be caught if no sudden movements were made.

The Current Chamber. The reactions of fish were noted when placed in a round aquarium containing a paddle wheel in the center, with about 4 in. of free swimming space between the ends of the paddle and the edge of the aquarium. The paddles were revolved at various speeds, setting up known current velocities.

Control fish acted in a characteristic manner when placed in the current chamber. As soon as they felt the water in motion, they oriented themselves to swim into the current. The swimming speed varied with the speed of the current so that at all times they maintained a fixed position relative to the nonmoving objects in the aquarium. Normal fish were not swept away by the paddle, nor did they overshoot their mark.

By means of the current chamber, it was possible to differentiate in the main between stimulation, tranquilization, and sedation. Sedated fish had poor control of motor ability and made no measurable response to the challenge of the current. The net result was that these fish were carried around by the paddle wheels in complete disorientation. Tranquilized fish, on the other hand, acted more like untreated controls. For example, fish treated with chlorpromazine could sense the current direction and were able to orient themselves properly. However, there was characteristically an inability to maintain the exact speed of the current, resulting in a slow but definite progression backwards as the current velocity was increased. Fish showing stimulation, as with pentylenetetrazol, were hyperactive and adjusted poorly to changes in current speed; when the current velocity was increased, the fish overcompensated and swam much too fast.

Blind fish, probably owing to their inability to fix their position optically, did not exhibit the same behavior as goldfish, and were swept away by the current and usually entangled in the paddles.

The Maze Test. Blind fish were observed in a maze consisting of a polyethylene pan about 25 cm. wide, 30 cm. long, and 20 cm. deep, with partitions of Plexiglas 3 mm. (⅛ in.) thick, as illustrated in figure 1.

Control blind fish swam through the maze in about 90 seconds. Since there was no stimulus or reward in these experiments, it was improbable that any conditioning of the fish occurred.

These genetically blind cave fish of Mexico have compensated for their lack of eyes by an increase in motor activity. Thus, by being in more places more times, they are assured of increased opportunity for food supply. When in an environment that contains no upsetting thermal, chemical, or physical stimuli, these fish swim at random.

Ataraxics increased the time necessary for the fish to run the maze completely. The

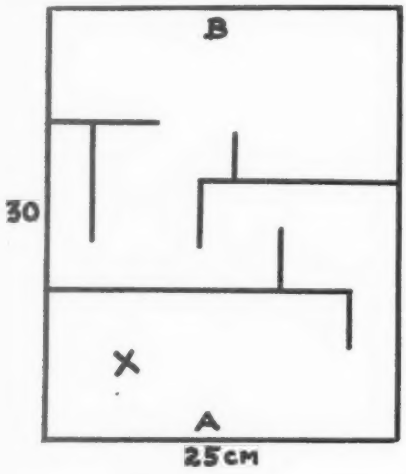

FIG. 1. Blind fish maze. Three blind cave fish are placed in section *A* of the maze at point *X*, and the end point is recorded as the time necessary for one fish to enter section *B*.

activity was decreased, but apparently not the randomness of the motion. Central nervous stimulants decreased the time of "running" the maze by increasing the over-all activity. The maze test was used as a semiquantitative measure of the effect of an ataraxic or stimulant.

RESULTS

The more characteristic effects with optimal species and the dosage and route of a number of drugs follow, grouped according to their general pharmacological classification.

Ataraxics. CHLORPROMAZINE. Gills: Goldfish and guppies, when placed in a solution of 6 μg./ml., rose to the surface within six to eight minutes, bubbled, and seemed to gasp for air. At this stage they could be handled and picked up easily when approached gently, but they avoided a strong or rapid stimulus. In the current chamber they were able to swim normally at moderate current velocities. At greater current speed they did not do as well as the controls. At the same concentration, blind fish were affected within two minutes and there was a fourfold increase in the time necessary to go through the maze.

BUCLIZINE. Gills: Goldfish showed no response to saturated solutions.

Injection: Goldfish reacted normally to most stimuli after the intraperitoneal injection of 0.25 Gm./Kg., but they could be handled and picked up if not frightened by abrupt motion. Their response to the current chamber was the same as that of the controls.

AZACYCLONOL (FRENQUEL). Gills: Guppies exposed to 100 to 200 μg./ml. solutions did not show any abnormalities for 12 to 15 hours, after which they darkened and lost control over swimming, although their pectoral fins could be moved. Death ensued within two days even after apparent recovery.

BENZACTYZINE (SUAVATIL). Gills: Guppies placed in solutions of 0.1 to 0.8 mg./ml. became agitated within one to four minutes. Darkening occurred in a light background,

and swimming became awkward. Within seven minutes at 0.2 mg./ml., the fish were uncoordinated and the pectoral fins were paralyzed, but swimming continued until death ensued. They recovered in approximately one hour if placed in fresh water at the onset of pectoral paralysis. Goldfish and blind cave fish placed in a solution of 0.1 mg./ml. exhibited reactions similar to those of the guppy, but did not show the primary agitation. Within 6 to 12 minutes, they were uncoordinated, swimming on their sides, and looping, with partial paralysis of the pectoral fins. A period of activation followed a slightly depressed state in blind fish, and they did as well as or better than controls in penetrating the maze. However, their movements were poorly coordinated and erratic as compared to normal controls.

HYDROXYZINE (ATARAX). Gills: Concentrations as low as 1 μg./ml. produced a darkening response in guppies in the presence of light after approximately two hours. Higher concentrations (5 μg./ml.) resulted in regurgitation, defecation, and apparent sedation, but with a violent spasmodic reaction to tactile stimuli. Concentrations of 10 μg./ml. telescoped these reactions and terminated with convulsions (and usually death) in 60 to 70 minutes.

Injection: Goldfish injected with 0.25 Gm./Kg. responded poorly to current after 10 minutes. Convulsions occurred in approximately 20 minutes, accompanied by an increase in respiratory movements and occasional darting around the tank (as if stimulated). Death followed shortly. At 0.15 Gm./Kg., agitation, activation, erratic behavior, and convulsions also occurred within 20 minutes, but over a period of about three hours the fish returned to normal. At a dose of 0.05 Gm./Kg., increased activity occurred within 20 minutes but with no other demonstrable effects.

Stimulants. PENTYLENETETRAZOL. Gills: Guppies and blind cave fish, when placed in a solution of 0.5 mg./ml. for 15 minutes, exhibited excitability and erratic swimming. Chlorpromazine did not counteract this activity in the guppies. The blind cave fish went through the maze in 25 seconds, about four times as fast as the controls.

Injection: Goldfish, at a dosage of 0.12 to 0.25 Gm./Kg. intraperitoneally, showed an increase of activity and peculiar writhing-like motion within 10 to 40 minutes. Partial paralysis, uncoordinated swimming, and convulsions occurred at higher doses. In the current chamber they consistently overshot their mark when the current velocity was increased.

CAFFEINE. Gills: Guppies became oversensitive, in 4 to 10 minutes, to tactile stimulation when placed in a concentration of 0.7 mg./ml. They were unable to keep up with the control guppies in the current chamber.

PIPRADOL (MERATRAN). Gills: Guppies placed in 50 to 200 μg./ml. solutions exhibited the following in 15 to 70 minutes: regurgitation, followed by excitability and pectoral paralysis, and an extremely light-colored body.

Psychotomimetics. BULBOCAPNINE. Gills: In solutions of 25 to 100 μg./ml., both guppies and goldfish became very active in 15 to 40 minutes and did poorly when placed in the current chamber. At higher concentrations, they showed signs of lack of control, swam erratically, and then had convulsions. After a day of recovery in fresh water, guppies could still be sent into convulsions by tapping the aquarium.

LYSERGIC ACID DIETHYLAMIDE. Gills: Guppies turned dark within 10 minutes after being placed in a solution containing 2 μg./ml. The effect lasted for approximately one hour, during which the experimental animals could be differentiated from the controls. On the other hand, goldfish exposed to the same solution reacted within 10 to 15 minutes by dorsal fin droop, floating at the surface, lessened response to current, and backward swimming, but they exhibited normal fear. Blind cave fish responded to this same concentration within one to four minutes by swimming in very small circles. This was followed by increased movements in all directions and, after 10 to 15 minutes, by a return to normal. It took these fish about five times as long as the controls to swim through the maze.

MESCALINE. Gills: This drug had no effect on guppies swimming in 100 μg./ml. No color change was noted.

Injection: Goldfish, when injected with 0.25 Gm./Kg., swam with short jerky movements and seemed excited. Current behavior was normal.

Autonomics. EPINEPHRINE BITARTRATE OR CHLORIDE. Gills: 0.1 mg./ml. gave no reaction.

Injection: Goldfish responded within 40 minutes to an injection of 0.25 Gm./Kg. by poor control over swimming, which seemed undirectional. Food was ignored. There was a fair response to tactile stimulation and the current chamber. In general, the animals seemed to be dulled in sensitivity and motor ability.

ACETYLCHOLINE HYDROCHLORIDE. Gills: Goldfish in 0.2 mg./ml. showed no reaction.

Injection: Goldfish injected with 0.5 Gm./Kg. intraperitoneally responded in four minutes by becoming quiet and resting on the bottom. This was followed by a loss of some control over swimming in about 20 minutes and a failure to keep pace in the current chamber.

Sedatives and Depressants. PHENOBARBITAL SODIUM. Gills: At concentrations of 1 mg./ml. in the swimming water, guppies reacted within 35 minutes (two hours for 0.4 mg./ml.) by darkening, slow swimming, and finally loss of control. Goldfish showed impaired motor ability and sedation within three hours. Blind cave fish were not affected by this concentration in three and one-half hours. At higher concentrations (5 mg./ml.), blind fish swam erratically in 40 minutes.

URETHANE. Gills: At concentrations of 3 mg./ml., guppies became dark and somewhat erratic within six minutes but they still responded normally in the current chamber. After 25 minutes, they no longer responded to any stimuli although they propelled themselves through the water. Blind fish, by four minutes, varied between resting motionless on their sides on the bottom (unconscious) and swimming erratically. When placed in fresh water, recovery was rapid, in 1 to 10 minutes, depending on the length of time in the test solution. Awakening initiated a period of high activity.

ETHYLENE GLYCOL. Gills: Goldfish in 2 per cent solution showed no effects.

Injection: Goldfish injected with 15 ml./Kg. acted abnormally after one hour with periods of complete cessation of movements alternating with periods of activity. After 24 hours, slight stimulation caused extreme activity.

ETHANOL. Gills: Guppies in a 1 per cent solution became dark in a light background within 20 minutes and swam unidirectionally. There was a reduced response to current.

Goldfish in the same solution were first quiescent and then active. When stimulated, there was response to a low threshold, but escape reflexes were uncoordinated.

DISCUSSION

Fish have been found to give a surprising array of signs from the administration of drugs. It is apparent that drugs that are stimulants in mammals are likely to be stimulants in fish, and vice versa. There appears to be enough variety within the group of stimulant or depressant manifestations in fish so that drugs in the same pharmacological category may sometimes be differentiated. The specificity of the different reactions for particular drugs has oftentimes been distinctive. Fish thus offer a valuable addition to higher animals as test objects for the assessment of new drugs with effects on the central nervous system.

The normal behavioral pattern for each species must be recognized, however, since a drug-induced effect in one species may resemble normal behavior in another. For instance, goldfish, after the administration of pentylenetetrazol, duplicate the high activity of blind fish and, after chlorpromazine, bubble at the surface like paradise fish. Also, although handling does not affect the fish appreciably, factors other than drugs can produce abnormal effects. Thus fin droop is a general symptom of poor physical condition, and fish may become pale from fright as well as from a light background. It is therefore obvious that proper choice of species and adequate controls are of prime importance.

The fact that drugs may enter a fish through the gill membrane or may be introduced directly by needle may be of use in the study of membrane permeability. It has been particularly interesting that drugs that easily enter through the gill membrane of one fish may not enter through the gill membrane of another.

SUMMARY AND CONCLUSIONS

Three species of fish, i.e., guppies, blind cave fish, and goldfish, were observed after the administration of various drugs affecting the central nervous system. General activity, response to the stress of a current of water, and to a maze test (blind fish) allowed characterization of various drugs. Ataraxics, sedatives, stimulants, and autonomic drugs produced in fish counterpart reactions to those observed in mice and higher animals. In some instances it was possible to observe characteristic differences between drugs of the same pharmacological type.

RESUMEN

Se estudiaron las reacciones de tres especies de pequeños peces de acuario, carpas, (*Lebistes reticulatus, Phoxinus phoxinus* y *Carasseus aureatus*) a diversas drogas que actúan sobre el sistema nervioso central. La actividad general, la respuesta al stress producido por una corriente de agua y la prueba del laberinto (*Phoxinus*) permitieron la caracterización de varias drogas. Los ataráxicos, sedantes, estimulantes y drogas que actúan sobre el sistema nervioso autónomo, causaron en el pez reacciones semejantes a las observadas en los ratones y animales superiores. En algunos casos fue posible observar características diferentes entre las drogas de un mismo tipo farmacológico.

RESUME

Trois espèces de poisson, *Lebistes reticulatus, Amblyopsis spelaeus* et *Crassius amatus,* ont été observées après administration de diverses drogues affectant le système nerveux central. L'activité générale, la réponse à un stress provoqué par un courant d'eau et, pour l'*Amblyopsis spelaeus*, le test du labyrinthe, ont permis la détermination de diverses drogues. Les ataraxiques, les sédatifs, les stimulants et les médicaments agissant sur le système autonome produisaient chez le poisson des réactions comparables à celles observées chez la souris et animaux plus grands. Dans certains cas il a été possible d'observer des différences caractéristiques entre médicaments d'un même type pharmacologique.

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A Trial of Oral Pentamethylenetetrazol in Senile Patients

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DANVERS, MASSACHUSETTS

A comprehensive placebo control study of the use of pentamethylenetetrazol in the treatment of patients with chronic brain syndrome was conducted by Mead et al.[2] Their investigation showed no significant clinical improvement in the drug-treated group as compared with those who received placebo medication. On the other hand, Kass and Brown,[1] Tennent,[5] and Smigel[4] continue to report that pentamethylenetetrazol is of value in patients having a chronic brain syndrome, as did the majority of previous investigators. The benefit was seen chiefly in the spheres of improved behavior and mood, although Kass and Brown[1] also reported a measurable psychometric improvement "in orientation, in ability to size up and comprehend a practical social situation and in associate learning of new and unfamiliar material." They further suggested a detrimental effect on visual reproduction and on attention and mental control needed for concentration. In view of these conflicting reports and because of the importance in firmly establishing any therapy of value for senile patients, a control study on the use of pentamethylenetetrazol in the treatment of senility is reported.

METHOD

The subjects consisted of 44 men patients in the Danvers State Hospital. These patients were selected and placed into two diagnostic groups, according to the criteria of Roth,[3] as follows: (1) Chronic brain syndrome, cerebral arteriosclerosis, with: Dementia associated with focal signs and symptoms indicative of cerebrovascular disease; or a remittent or markedly fluctuating course at some stage of the dementing process, plus any one of several features (emotional incontinence, preservation of insight, or epileptiform seizures). (2) Chronic brain syndrome, simple senile deterioration: A condition with a history of gradual and continually progressive failure in common activities of everyday life and a clinical picture dominated by failure of memory and intellect and disorganization of personality, where these are not attributable to specific causes such as infection, neoplasm, chronic intoxication, or cerebrovascular disease.

The two groups were used because a difference in response would help to delimit the indication for pentamethylenetetrazol and would serve as an indicator as to the possible site and mode of action, which are still highly controversial. Finally, an improvement in the senile deterioration group would be more significant in view of the normal fluctuations known to occur in the mental functions of cerebral arteriosclerotics.

It is, of course, true that the clinical picture is seldom a pure one and that some overlap inevitably occurs. Nevertheless, so far as possible, patients who fitted a pure picture were selected. The patients, as a group, were rather deteriorated; again this meant that the significance of changes would be greater.

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TABLE I
Age Ranges of Treated and Control Patients

	Cerebral arteriosclerosis	Senile deterioration
Number of patients	24	20
Age range	58–88	67–88
Mean age		
Control	79	79
Pentamethylenetetrazol	71	78

Ages ranged as shown in table I.

The patients in each group were allotted numbered discs. The discs were selected at random from a shaker and placed alternately in the placebo or pentamethylenetetrazol group.

The following group of tests was employed: (1) Psychological tests: Comprehension subtest of the Wechsler Adult Intelligence Test; Wechsler Memory Scale; Form Board of the Revised Minnesota Paper Form Board Test; Behavior Rating Scale (a modified hospital behavior rating scale that rated 17 functions on a six point scale in two directions; the patients were rated by two trained clinical psychologists, and their ratings were averaged). (2) Clinical evaluation: This was based on a standard type of interview for all patients. They were assessed as: "better," "unchanged," or "worse." (3) Nursing staff evaluation: The person in charge of each of the three eight hour shifts was asked to evaluate as "better," "unchanged," or "worse" the following: General condition, ease of management, appetite, noisiness, and cleanliness. In the case of "sleep," only the two night shift evaluations were used. In all cases the average opinion was taken. The psychological tests and the clinical evaluation were performed on all the patients before the institution of therapy and afterwards; the nursing staff evaluation was carried out only afterwards. Only the pharmacist was aware of which group was taking metrazol or placebo until all the tests and evaluations were completed.

The dosage of pentamethylenetetrazol was 0.3 Gm. three times a day during waking hours. Administration was continued for six weeks, with the final testing and evaluation being carried out in the sixth week while the patients were still on medication.

RESULTS

Four patients died during the course of the trial. Two died from heart failure (1 on placebo and 1 on pentamethylenetetrazol), and 2 died from bronchopneumonia (1 on placebo and 1 on pentamethylenetetrazol). This left 9 patients in each senile deterioration group and 11 patients in each cerebral arteriosclerotic group.

Psychometric Tests. Because the distribution of the psychometric test results was skewed, nonparametric tests were used in the statistical analyses.[6] No direct comparison between the groups of pentamethylenetetrazol and placebo patients was made because of the marked individual differences in the pattern of test performances. The performance of each patient

TABLE II

Physicians' Classification of Patients' Clinical Status After Pentamethylenetetrazol or Placebo

	Pentamethylenetetrazol			Placebo		
	Better	Unchanged	Worse	Better	Unchanged	Worse
Cerebral arteriosclerosis	5	4	2	2	7	2
Senile deterioration	1	7	1	1	7	1

on the four tests before pentamethylenetetrazol or placebo was compared with his performance after receiving either pentamethylenetetrazol or placebo. In general, in both the pentamethylenetetrazol and placebo groups the results reveal great variability. Some patients improved on the second testing, some worsened, and some remained the same with no consistent trend evident. A specific analysis indicated that neither pentamethylenetetrazol nor placebo altered the patients' performances on any of the psychological tests

TABLE III

Nurses' Classification of Patients' Clinical Status After Pentamethylenetetrazol or Placebo

	Pentamethylenetetrazol			Placebo		
	Better	Unchanged	Worse	Better	Unchanged	Worse
Management						
Cerebral arteriosclerosis	1	10	—	3	7	1
Senile deterioration	1	7	1	2	7	—
Appetite						
Cerebral arteriosclerosis	1	10	—	—	11	—
Senile deterioration	—	9	—	—	9	—
Sleep						
Cerebral arteriosclerosis	2	9	—	2	9	—
Senile deterioration	—	9	—	2	7	—
Noisiness						
Cerebral arteriosclerosis	—	11	—	—	11	—
Senile deterioration	—	9	—	1	8	—
Cleanliness						
Cerebral arteriosclerosis	—	11	—	—	11	—
Senile deterioration	—	9	—	1	8	—
General condition						
Cerebral arteriosclerosis	—	11	—	3	8	—
Senile deterioration	1	8	—	3	6	—

to a statistically significant degree. It is worth noting that, rather than improvement, there was a tendency for the senile deterioration group on pentamethylenetetrazol to worsen in performance on the Form Board, with 6 out of 9 patients in this group obtaining lower scores on the second trial.

Clinical Evaluation. The clinical examinations did not reveal any positive evidence of improvement in either group. One trend toward improvement was noted in the cerebral arteriosclerotic group on pentamethylenetetrazol. Some of these patients did appear more alert and talkative, but at the same time this was not productive and hence was not reflected in other behavioral improvement.

A statistical comparsion of the clinical judgments with an average assessment of each patient culled from the psychometric tests showed these two independent evaluations to be reasonably in agreement. The chi square test yielded a P value of 0.1 for the senile deterioration group and of 0.12 for the cerebral arteriosclerotic group. A disagreement in evaluations occurred over several cases judged clinically unchanged while performing worse on the tests. (See table II.)

Nursing Evaluations. As may be seen from table III, the great majority of cases showed essentially no change in any of the functions rated. The reports that appetite improves in pentamethylenetetrazol-treated patients were not confirmed.

SUMMARY

A placebo control study of the effects of oral pentamethylenetetrazol in 44 senile patients, 20 of whom were diagnosed as having a brain syndrome with senile deterioration and 24 of whom were diagnosed as having a chronic brain syndrome with cerebral arteriosclerosis, is described. Psychometric tests, a rating scale, and physicians' and nurses' clinical evaluations were used to appraise changes. There was no significant improvement with pentamethylenetetrazol or placebo in either the arteriosclerotic or senile deterioration groups for any of the measures used. It is concluded that pentamethylenetetrazol is not of value in senile patients who show any definite degree of deterioration.

ACKNOWLEDGMENTS

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RESUMEN

Se describe en este trabajo un estudio sobre los efectos del pentametilentetrazol por vía oral en 44 pacientes seniles. En 20 se hizo el diagnóstico de síndrome cerebral con deterioro senil; y en 24 se diagnosticó un síndrome cerebral crónico con arterioesclerosis cerebral. Para determinar las variaciones experimentadas por los pacientes, se usaron pruebas psicométricas, una escala de evaluación y las opiniones clínicas de médicos y enfermeras. No hubo mejoría significativa con pentametilentetrazol o placebo en ninguno de los pacientes con arterioesclerosis o con deterioro senil. Se llegó a la conclusión de que el pentametilentetrazol no es de valor para los pacientes seniles que muestran un grado definido de deterioro mental.

RESUME

Description d'une étude-témoin avec placebo effectuée pour déterminer les effets du pentaméthylènetétrazol oral chez 44 malades séniles; on avait porté le diagnostic de syndrome cérébral avec détérioration sénile chez 20 d'entre eux et, chez 24, celui de syndrome cérébral chronique avec artériosclérose cérébrale. Les tests psychométriques, l'évaluation selon un certain niveau d'échelon et l'évaluation clinique par les médecins et les infirmières ont été utilisés pour l'estimation des changements. Aucun degré d'amélioration significatif n'a succédé à l'administration de pentaméthylènetétrazol ou de placebo, tant dans le groupe de l'artériosclérose que dans celui de la détérioration sénile quel que soit le mode de détermination utilisé. L'auteur considère que le pentaméthylènetétrazol est sans valeur chez le malade sénile en présence d'un degré défini de détérioration cérébrale.

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Second Annual Meeting of the Society for the Scientific Study of Sex

The Society for the Scientific Study of Sex will hold its second annual meeting on November 7, 1959, at the Barbizon Plaza Hotel, New York City. There will be two symposia, entitled "What is Sexually Normal?" and "Psychological Factors in Infertility." Details of the meeting can be obtained from Robert V. Sherwin, Executive Secretary, Suite 704, 1 East 42nd Street, New York 17, N. Y.

The aim of the society is to bring together scientists working in the biologic, medical, anthropologic, psychologic, sociologic, and allied fields who are conducting significant sexual research or whose profession confronts them with sexual problems.

Intravenous Administration of PM 1090: Clinical Experience with a New Convulsant Drug

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PM 1090† is chemically described as α,α-β,β-tetramethyl succinimide and has the structure shown in figure 1. It has been demonstrated that PM 1090 is a powerful convulsant drug in the oral form, free of toxic effects other than occasional nausea and vomiting.[1] There was complete amnesia for seizures induced by PM 1090, and there was no unpleasant aura associated with administration of the drug. However, with oral medication it was impossible to predict just when a patient was going to have a grand mal seizure. It was necessary to keep patients under constant observation while they received the drug.[2]

This pilot study was undertaken to investigate the use of intravenous PM 1090 as a practical convulsive therapy. The drug was administered two or three times a week in a concentration of 10 mg./ml. of solution. Intramuscular chlorpromazine, 50 mg., was given one-half hour before treatment to reduce the incidence of postseizure nausea. Phenobarbital, 1 gr., was added one hour after treatment as an anticonvulsant.

Each patient had a routine pretreatment work-up consisting of a physical examination, spine roentgenogram, complete blood count, and electroencephalograms (EEG). Some of the patients were followed up with frequent EEG's during and after the period of treatment until their EEG's returned to the pretreatment state. Only patients in good physical condition were used in this study, although the only known contraindications to the use of PM 1090 are those related to the physical effects of a grand mal seizure.

Patients receiving PM 1090 continued on a regular active treatment program on the ward, consisting of occupational therapy and ward and recreational activities. Chlorpromazine was continued in those patients who had been receiving it. Home visits were restricted during the treatment period because of the possibility that the patient might sustain an unwelcome seizure and also because experience with the drug was limited.

A 32 bed intensive treatment ward was used for this study. A 16 bed electroshock therapy recovery room is connected to this ward. PM 1090 was administered in the recovery room. Ward personnel consisted of a charge nurse and two attendants. Patients receiving electroshock therapy were also housed on this ward.

Seventeen woman patients ranging in age from 20 to 56 years received a six to eight week course of treatment with PM 1090. Most of the patients were chronically ill schizophrenics. All except 2 patients had received one or more courses of electroshock therapy;

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† PM 1090 was supplied through the courtesy of Parke, Davis & Co.

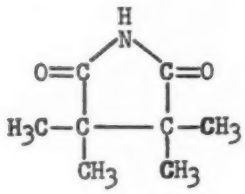

FIG. 1. Structure of PM 1090.

all the patients had received reserpine or chlorpromazine with little improvement. A course of treatment usually consisted of 10 to 15 grand mal seizures.

Patients were given from 70 to 200 mg. of PM 1090 intravenously, usually twice a week. The drug was administered with the patient lying in bed. A rubber mouth gag was inserted just before the drug was injected. One person held the mouth gag in place; another one held the patient very lightly during the seizure. The drug was injected rapidly, usually in 15 seconds or less. A grand mal seizure usually ensued within 30 seconds after the injection of the drug.

Each patient had her own characteristic seizure pattern, but certain observations may be made. As a rule, generalized myoclonic twitching terminated in a strong tonic contraction and the grand mal seizure. Some patients became unconscious immediately before going into the tonic phase of the grand mal seizure. Others became restless and cried out immediately prior to the tonic contraction. If the amount of the drug given was not sufficient to produce a grand mal seizure, the early phase of the seizure was usually indicated by myoclonic twitching, which subsided rapidly. Subjectively, patients who did not lose consciousness reported a feeling of dizziness as if they were about to "go under." There was no unpleasant aura associated with injection of the drug even if the patient did not sustain a grand mal seizure. Apprehension was associated with the idea of intravenous medication—apprehension did not increase after the drug was injected. Many of the patients reported that treatment with PM 1090 was preferable to a course of electroshock therapy. No patient felt that PM 1090 was more unpleasant than electroshock therapy.

Postseizure amnesia was marked. Patients were unable to recall anything that happened after the drug was injected. Patients who were extremely apprehensive and fearful at first became less apprehensive after a few treatments.

Patients became moderately confused during the latter weeks of treatment. Those who showed the greatest degree of clinical improvement were most aware of feeling confused. As one patient expressed it, "If my head wasn't screwed on, I'd lose it." At this stage of treatment, the patient was also unable to recall disturbing ideas. This confused state was accompanied by mood changes of two types: (1) Patients became hostile and demanding or (2) mildly euphoric with apparent lack of concern for personal appearance.

The EEG reaction exhibits practically every feature seen in the EEG patterns of epileptics. (This will be the subject of a separate paper.)

A total of three untoward grand mal seizures occurred in 3 of the patients. The seizures occurred a few hours after the morning treatment. This phenomenon was controlled by

the use of phenobarbital, 1 gr., following treatment. As observed with oral PM 1090, there were no serious toxic reactions to intravenous PM 1090. Patients infrequently complained of mild nausea or a headache.

Analysis of results immediately upon completion of the course of treatment proved to be of limited value in evaluating possible therapeutic effects of PM 1090. All patients improved, even if only to a slight degree, while on treatment. Records on each patient were examined six months or longer after completion of a course of PM 1090. Change in the condition of the patient was determined on a functional basis. "Markedly improved"

TABLE I

Data on Individual Patients

Case, age	Diagnosis and duration of illness	Previous somatic therapy	Maximum dosage, mg., I. V.	No. of grand mal seizures	Results
1. N. B., 22	Schizophrenic, paranoid, 8 years	EST	100	3	Markedly improved
2. B. B., 51	Schizoaffective, 6 years	EST, insulin, atropine	120	14	Temporarily improved
3. P. C., 32	Schizophrenic, chronic undifferentiated, 9 years	EST, insulin	140	15	Unimproved
4. C. C., 36	Schizophrenic, chronic undifferentiated, 7 years	EST	190	18	Unimproved
5. S. D., 46	Schizoaffective, 15 years	EST	140	11	Improved
6. V. M., 35	Schizophrenic, chronic undifferentiated, 6 years	EST, insulin	90	10	Improved
7. M. F., 25	Schizophrenic, catatonic, 1 year	EST	90	14	Markedly improved
8. J. R., 49	Schizophrenic, paranoid, 5 years	None	90	9	Improved
9. E. F., 39	Schizophrenic, chronic undifferentiated, 6 years	EST	120	11	Markedly improved
10. C. F., 30	Schizophrenic, chronic undifferentiated, 7 years	EST, atropine	100	17	Unimproved
11. M. K., 27	Schizophrenic, chronic undifferentiated, 4 years	EST	125	13	Improved
12. E. J., 49	Schizophrenic, paranoid, 4 years	EST	140	16	Temporarily improved
13. I. G., 44	Schizophrenic, chronic undifferentiated, 17 years	EST, insulin, atropine	160	13	Improved
14. C. G., 50	Involutional psychotic, 7 years	EST	200	12	Markedly improved
15. H. P., 54	Schizophrenic, chronic, undifferentiated, 11 years	EST, atropine	120	12	Markedly improved
16. N. D., 38	Schizophrenic, chronic undifferentiated, 7 years	None	130	15	Improved
17. G. M., 46	Schizoaffective, 10 years	EST	160	15	Markedly improved

TABLE II

Summary of Functional Condition of Patients Following Treatment

Classification	No. of patients
Markedly improved	6
Improved	6
Temporarily improved	2
Unimproved	3
Worse	0

refers to patients who are out of the hospital, many of whom no longer exhibit any signs of illness. "Improved" refers to patients who are more comfortable in the hospital. These patients are working and participating in hospital activities, whereas they were formerly sitting idly on the ward or were actively agitated and suicidal. "Temporarily improved" refers to patients who improved dramatically, but who relapsed within three months after finishing a course of treatment. "Unimproved" refers to patients whose mental condition remained essentially unchanged, although brief improvement was noted while they were receiving PM 1090. These results are summarized in tables I and II.

CASE HISTORIES

Four case histories are presented to illustrate the effects of PM 1090 on patients in each of the categories described.

Case 1: This patient was a white woman, aged 25, who had been hospitalized for one year. The diagnosis was schizophrenic reaction, predominantly catatonic type. The patient was unkempt and sat and stared most of the time. She had fixed delusions about being pregnant. She had responded poorly to a course of electroshock therapy one year earlier. On chlorpromazine she became less hostile, but her condition was otherwise unchanged. She continued to receive 100 mg. of chlorpromazine three times a day during her course of PM 1090.

This patient received a total of 15 treatments of PM 1090 and sustained 14 grand mal seizures. The dosage of PM 1090 ranged from 80 to 90 mg. As treatment progressed, she became more cheerful and active. This was followed by a state of confusion, when she was less certain of her delusions. Marked improvement continued following completion of the course of PM 1090, and in less than three months she was out of the hospital. Routine follow-up in the Out-Patient Department indicates that this patient is free of psychotic symptoms six months after her release on convalescent status.

Case 2: This patient was a white woman, aged 44, who had been ill for 17 years. The diagnosis was schizophrenic reaction, chronic undifferentiated type. The patient just sat most of the time and complained of noises in her head. She exhibited no interest in doing anything. Previous somatic therapy included electroshock therapy, insulin coma, and atropine, all to no avail. The patient received a total of 23 PM 1090 treatments, with 13 grand mal seizures. The dosage of PM 1090 ranged from 70 to 160 mg. Gradually the patient became more sociable, was less apathetic, and was able to participate in the work program. Over a period of six months she has maintained this level of adjustment in the hospital. Her thought content remained unchanged.

Case 3: This white woman, age 49, had been ill for four years. The diagnosis was schizophrenic reaction, paranoid type. The patient had numerous fixed somatic delusions and kept insisting that life wasn't worth living if she had to suffer such pain at the hands of others. She was agitated, extremely hostile, and also suicidal. Two previous courses of electroshock therapy had only added to her paranoid delusional system. On chlorpromazine she was less hostile but otherwise unchanged. One hundred milligrams of chlorpromazine three

times a day was continued during her course of PM 1090. The patient received a total of 23 PM 1090 treatments, sustaining 16 grand mal seizures. The dosage of PM 1090 ranged from 70 to 140 mg. There were bitter paranoid complaints prior to each treatment, but later in the day the patient could not recall having had a seizure. For a while, she seemed to improve remarkably. Weight gain, more cheerful affect, and interest in hospital activities were noted. The patient was able to hold a hospital privilege card. Paranoid ideation and somatic delusions were only temporarily suppressed, and within three months she had relapsed to her previous condition.

Case 4: This white woman, age 32, had been ill nine years. The diagnosis was schizophrenic reaction, chronic undifferentiated type. The patient was agitated and hostile, threatening suicide and refusing to eat. She was also autistic and withdrawn. Intensive treatment with electroshock therapy, insulin coma, and chlorpromazine, as well as psychotherapy, resulted in only temporary remissions of her illness. She became more actively disturbed after two PM 1090 treatments, so she was again started on 100 mg. of chlorpromazine four times a day along with a course of PM 1090. She received a total of 18 PM 1090 treatments, with 15 grand mal seizures. The dosage of PM 1090 ranged from 90 to 140 mg. Some improvement was noted during her course of treatment. She was no longer a feeding problem. She took more interest in her personal appearance and was almost talkative for a while. As soon as the immediate effects of PM 1090 wore off (this took about two weeks), she returned to an apathetic, withdrawn state. The only change that could be noted was that the patient had gone from a relatively acute phase to a more chronic phase of her illness.

DISCUSSION

The results of this pilot study were interesting not only from a clinical but also from an experimental point of view. PM 1090 appears to be a relatively nontoxic drug. It was well tolerated by our patients when used intravenously. In most instances a grand mal seizure was readily produced within 30 seconds following rapid intravenous injection. Even if a grand mal seizure failed to ensue on a given occasion, the patient did not become disturbed and some benefit was apparently derived from the treatment. There was no unpleasant aura preceding the seizure. This form of convulsive therapy was less frightening than electroshock therapy for many patients. Treatment can be administered with the patient lying in bed. The only equipment needed is the mouth gag, syringe, and needle.

Therapeutic results certainly suggest that further clinical investigation with PM 1090 is warranted. The prognosis for these patients was poor, yet 6 of the 17 are now out of the hospital. Patients responded to PM 1090 at least as well as they had to electroshock therapy. Several of the patients who had responded poorly to electroshock therapy improved markedly following PM 1090, suggesting that the therapeutic effect of the two types of convulsive treatment may not be identical. Patients could continue to receive chlorpromazine, when necessary, without ill effect. In no instance did a patient become worse following a course of intravenous PM 1090.

Experimentally, and perhaps diagnostically, PM 1090 should be useful in the investigation of convulsive disorders. PM 1090 lowers the seizure threshold, and a variety of myoclonic seizure phenomena may be produced. Individual variations were noted both as to the amount of PM 1090 required to produce a seizure and as to the pattern of the seizure.

SUMMARY

A course of convulsive treatment with PM 1090 was undertaken with 17 chronically ill schizophrenic woman patients. Twelve of the 17 patients remained significantly improved

six months after completion of a course of treatment with this drug. It is suggested that PM 1090 is safe, effective, and easy to use intravenously. PM 1090 is apparently free of unpleasant aura, and it was well tolerated by the patients. Further clinical and experimental investigation with PM 1090 is recommended.

RESUMEN

Se llevó a cabo un curso de tratamiento convulsivante con PM 1090 en 17 mujeres esquizofrénicas crónicas. Doce de estas 17 pacientes continuaron significativamente mejoradas seis meses después de haberse completado el tratamiento. Se sugiere que el PM 1090 es innocuo, eficaz y fácil de administrar por vía intravenosa. Aparentemente no produce aura incómoda. El medicamento fue bien tolerado por los pacientes. Se recomienda nueva investigación clínica y experimental con PM 1090.

RESUME

Une série de traitements convulsivants à l'aide de PM 1090 a été entreprise chez 17 femmes atteintes de schizophrénie à l'état chronique. Parmi ces 17 malades, 12 ont conservé l'amélioration acquise pendant six mois, après une série de traitements avec cette drogue. L'auteur considère que PM 1090 est inoffensif, efficace et facile à administrer par voie intraveineuse. PM 1090 ne semble pas provoquer d'aura désagréable et il a été très bien toléré par les malades. Une plus ample investigation clinique et expérimentale du PM 1090 est conseillée.

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Eighth Annual Alfred Korzybski Memorial Meeting

The Eighth Annual Alfred Korzybski Memorial Meeting, to be held April 11, 1959, at the Carnegie International Center, 345 East 46th Street, New York City, will feature, among others, Professor William J. Fry, of the University of Illinois, on his work with ultrasound in neurology, and Professor Charles M. Pomerat, University of Texas, whose studies have revealed hitherto unsuspected dynamics of cellular elements of the nervous system. Reservations may be sent to the Institute of General Semantics, Lakeville, Conn., sponsor of the meeting.

Perphenazine Treatment in Psychotics

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Perphenazine (Trilafon) is a new derivative of chlorphenothiazine with characteristics resembling those of the phenothiazines that are already well established as effective ataraxics. A score or more papers describing its use and effects have already appeared in the psychiatric literature. The present study confirms previous observations and sheds new light on treatment with this powerful new ataraxic.

The study was made in a large state hospital cottage with five units or subdivisions housing 640 chronically disturbed woman patients. For years a great deal of electric shock therapy (in some as many as 1000 treatments), sedation, restraint, and seclusion had been used. Many of the patients had been sent to the cottage with the belief that their severe management problems could be handled best in the new well-equipped and well-staffed building. Many had been extremely disturbed for a long time, and most were treatment failures. The majority were chronic schizophrenic patients, and a few had been lobotomized; but they were selected for perphenazine treatment without considering diagnosis or previous treatment. All kinds of patients were included, such as epileptic, senile, arteriosclerotic, post-traumatic, mental defective, and those with affective states. Twelve per cent of the patients had been hospitalized for six months to two years; 13 per cent two to four years; 14.8 per cent from four to eight years; and 60.2 per cent more than eight years. Medical and nursing personnel had become familiar with other ataraxics, and they used perphenazine as the latest one available. The patients were divided in two groups: in the first they were aggressive, assaultive, destructive, and excitable; and in the second they had become vegetative, withdrawn, and seclusive.

During a 10-month period, 363 of these patients were treated with perphenazine and were observed closely. Complete records were made of their treatment, behavior, and ultimate disposition.

Table I shows that 80 per cent of the 363 in this survey used 32 mg. or less daily, 97.27 per cent used 64 mg. or less, and 2.7 per cent took from 96 to 320 mg. daily. The last group did not suffer from ill effects even though large amounts were used. Ayd and Taylor found 32 to 96 mg. of perphenazine to be the average initial daily dose in two private mental hospitals.[1] Ayd reported that 16 to 64 mg. was the average daily dose in 300 acutely disturbed patients, with the maximum dose seldom exceeding 100 mg.[2]

Table II shows the duration of treatment. Although 16 per cent used perphenazine for only a month or less, 21 per cent used it for 10 or more months, and two thirds of the group used it for varying periods in between.

Table III shows that 10 per cent of those using perphenazine also took small amounts of other ataraxics. Meprobamate was used in 3 per cent of patients to overcome the muscular

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TABLE I
Daily Dosage

Mg.	No. of patients	%
8 or less	77	21.2
16 or less	131	36.1
32 or less	84	23.14
48 or less	38	10.5
64 or less	23	6.33
96	3	0.8
128	4	1.1
320	3	0.8
Total	363	

stiffness and pain that may appear early in perphenazine treatment. It was of little value, and, since the symptoms subsided as the patients got used to perphenazine, meprobamate was discarded quite early in the survey. Reserpine, prochlorperazine, and chlorpromazine were used in small doses early in the study in only a few patients to gain experience in combining perphenazine with other ataraxics. Oversedation has been noted with other ataraxics, and stimulants such as dextroamphetamine have counteracted it. It was used for this reason in a very small percentage of our patients, so small as to be statistically insignificant; but it was found very early in the study that it was not needed if less perphenazine was used or if the larger doses were given later in the evening. Iproniazid was tried in 4 patients for a few weeks for depressive components in their illnesses, but none benefited and the drug was discontinued quite early in the study.

Side effects must be reckoned with in using ataraxics. For example, Atkinson reported toxic reactions in 28 per cent of 85 patients using promazine.[3] It is not surprising, therefore, that O'Reilly et al emphasized freedom from side effects in describing experiences with

TABLE II
Duration of Treatment

Medication, mo.	No. of patients	%
1	59	16.25
2	33	9.1
3	22	6.1
4	26	7.2
5	39	10.7
6	26	7.2
7	34	9.3
8	12	3.3
9	35	9.3
10	77	21.2

TABLE III

Use of Other Medications

Medication	No. of patients	%
Meprobamate	11	3.0
Reserpine	4	1.1
Chlorpromazine	20	5.5
Prochlorperazine	2	0.5
Iproniazid	4	1.1

perphenazine.[4] Ayd commented that side effects were transient, seldom serious, and usually elicited only upon direct inquiry.[2] In this study, side effects were found to be frequent but not troublesome in a hospital setting.

Table IV shows how often side effects appeared. The symptoms varied considerably and, since some patients suffered from more than one, double entries are common, as the record reflects the frequency of symptoms rather than the number of patients having complications. About 20 to 25 per cent are multiple entries. The comparative frequency (38 per cent) of the parkinsonian symptom complex probably distorts the treatment picture, since all the patients in this survey were women, and extrapyramidal symptoms complicate the use of other ataraxics in women twice as often as in men. Freyhan emphasized this in evaluating the complications of chlorpromazine and reserpine treatment in 653 mixed chronic patients.[5] The incidence of parkinsonism with these two drugs in his mixed group was 10.7 and 16.9

TABLE IV

Complications

Symptom	No. of patients	%
Overactive and irritable	7	1.9
Parkinsonism	139	38.3
Confusional state	2	0.5
Constipation	35	6.4
Blurred vision	4	1.1
Muscular aches and pains	19	5.2
"Cold and chilly"	14	3.9
Nausea and/or vomiting; not eating	9	2.5
Dizziness and fainting	10	2.8
Skin rashes	10	2.8
Edema (face, ankles, etc.)	12	3.4
Dry throat	10	2.8
Mild and moderate toxic reactions	4	1.1
Severe toxic reactions (shocklike state)	4	1.1
Difficult swallowing	4	1.1
Convulsive seizures	5	1.4
Depressed granulocytes	3	0.8

per cent respectively. Thus extrapyramidal symptoms surely would have been less frequent if there had been men patients in the group reported here.

The full-blown picture of parkinsonism appears rarely; usually only one or two of the manifestations were seen, such as rigidity, tremulousness, salivation, and gait disturbances. A few patients had two manifestations, and occasionally one had three. When muscular rigidity appeared, it was usually felt first in the neck and shoulders. Standard medications were used for these symptoms. Two milligrams of Artane, 2.5 mg. of Pagitane, or 2 mg. of Cogentin three times a day brought relief; and the dosage of perphenazine was not changed if this was effective. After the antiparkinsonian medications were discontinued, the patients could often take equally large doses of perphenazine without developing extrapyramidal symptoms again. Muscular aches and pains subsided with the use of aspirin and massage; only rarely was the dose of the drug reduced for this reason. The symptom was fleeting, usually clearing up after the first few weeks of treatment. Constipation yielded to the usual methods of treatment, presenting no special problem in spite of its frequency. O'Reilly noted slight lowering of systolic and diastolic blood pressure;[4] almost 3 per cent of our patients got dizzy, with 1 or 2 fainting on rare occasions, but their blood pressure seldom was low, and never lower than 110 mm. of Hg systolic pressure. Perphenazine thus has a distinct advantage over other ataraxics; hypotension is not a problem in its use. The depression in granulocytes in less than 1 per cent of the patients is similar to experiences with other phenothiazines; medication was discontinued, and no serious results ensued.

Four per cent of patients complained of feeling cold and chilly. These symptoms usually subsided with symptomatic treatment, but 4 patients went into a severe shocklike state requiring intensive emergency treatment on the infirmary ward. After feeling chilly for a day or two, they became stuporous. The condition resembled the shocklike state seen previously when using other ataraxics. The onset was not related to the amount of perphenazine used, the condition appearing after 25 to 64 days of treatment with daily doses of 12 to 64 mg. When unconsciousness was profound, the corneal reflexes were abolished and a prolonged convulsion would occur, then another in a few minutes, followed by deep sleep. Throughout this critical period, the blood pressure was scarcely altered, dropping no more than 5 to 15 mm. The pulse went up to 120 per minute, remaining full and steady, never thready or weak. All the while the patients salivated profusely and were bathed in perspiration. At no time could they be roused. Toward the end, patients curled up with limbs flexed and rigid. They could be roused from this peculiar state with barbiturates, given intramuscularly every four hours. Two to four injections sufficed, and the convulsions stopped with the first injection if they had not already ceased before. In three or four days, the patients emerged completely from this state and remained very quiet for a few weeks. Subsequently, when again disturbed, 2 of these patients were given perphenazine and 2 prochlorperazine without any ill effects.

Only 1 patient had to stop taking perphenazine because of excessive dreaming. Depression did not set in as a complication of perphenazine treatment, as is seen occasionally with other ataraxics. A few patients said they felt weak and listless, reflecting the chem-

ically induced decrease in psychomotor activity; but this symptom was noticed as a rule in the patients who had been most excited and hyperactive. It was really a letdown due to tranquilization; the condition had none of the criteria of a true depression, and it was disregarded. Iproniazid was used earlier in the survey for depression existing before perphenazine was given, but it was discontinued after it failed to relieve the few using it.

Since phenothiazine preparations help overcome nausea and vomiting in many disorders, it is strange that 9 patients (2.5 per cent) taking perphenazine for a mental disorder should become nauseous while using it. Both nausea and vomiting stopped in a few weeks, but it was necessary to lower the dose in half the cases. Ayd also refers to this form of epigastric distress.[2]

Jaundice figures prominently in the discussion of side effects with other ataraxics, but it does not appear with perphenazine according to the literature. In this study jaundice was never observed, nor was it found in the patients using perphenazine in other parts of the hospital who were not in this study.

Ayd observed no skin rashes in 300 neurotics and psychotics aged 16 to 80,[2] but there were 10 patients (2.8 per cent) in the current study of 363 psychotics who developed rashes.

In Freyhan's group of 653, medication was discontinued in 4.8 and 7.1 per cent respectively of those treated with chlorpromazine and reserpine.[5] In our study, table V shows that medication was discontinued in 20 patients (5.6 per cent) because of side effects and complications. Perphenazine was withheld when 3 patients became too overactive and irritable while using the drug, and when 3 others failed to be relieved from severe parkinsonism with large doses of conventional antiparkinsonian drugs. It was stopped in 4 who developed the previously described severe shocklike reaction; but they subsequently took perphenazine and prochlorperazine with no difficulty. In another 3 patients whose blood granulocytes were depressed, perphenazine was discontinued to avoid more serious complications. Convulsions appearing with use of ataraxics may be serious. Kurtzke had the unusually high incidence of convulsions in 6 patients out of 21 using promazine,[6] but in this study only 5 of the 363 patients had fits, and perphenazine was discontinued because of convulsions in two instances. This is similar to the experience of Fazekas in a study of 3000 acutely psychotic patients being treated with chlorpromazine and promazine.[7]

Table V shows that 74.7 per cent of the patients improved, 14.3 per cent did not change, and 5.5 per cent got worse with perphenazine treatment. Although the rate of improvement was high, only 7.7 per cent left the hospital. Others could have left if more adequate social resources had been available. For example, a broader family care program in the hospital might have provided homes for some patients without social resources. Inability to place them extramurally made it necessary for them to live, instead, in other parts of the hospital. Even so, improvement in such a large percentage benefited all patients on the unit, even those not getting the drug, since improved living conditions on the ward made life more agreeable for all. In fact, improvement in the ward's milieu rivaled in value the discharge of 7.7 per cent of its patients.

Earlier experiences with other tranquilizing drugs revealed individual peculiarities worth remembering in selecting ataraxics best suited for various types of patients, and such ob-

TABLE V
Results of Treatment

	No. of patients		%	
Improved	271		74.7	
Marked		56		15.4
Moderate		95		26.2
Mild		120		33.1
Unimproved	52		14.3	
Worse	20		5.5	
Discontinued (complications)	20		5.5	
Total	363		100.0	
Discharged	28		7.7	

servations also were made in the use of perphenazine. It was found that patients usually responded more quickly to this drug than to others, and that undesirable behavior was altered much earlier. Doses as low as 8 mg. twice a day some times accomplished this even in the first few days of treatment. Drowsiness and lethargy are distressing side effects in using ataraxics, especially when large amounts are needed to control behavior disturbances. The patients' alertness consequently suffers, and stimulants may be needed to counteract it. With perphenazine this was not necessary. The absence of drowsiness and lethargy and the speed of response enabled patients to participate in the ward's rehabilitation programs much earlier in the course of treatment.

Settel describes perphenazine as a "safe and valuable agent in the control of agitation among geriatric patients,"[8] reporting good or excellent results in 85 per cent of 60 patients 60 to 93 years old. Observations in our study fail to confirm this. The prevalent opinion at Stockton State Hospital had been that elderly patients respond better with promazine than other, more potent, ataraxics, and our study has not changed this opinion. Senile patients did not respond to perphenazine as well as the vigorous, disturbed, younger people. It would seem that older patients do not need such a potent ataraxic.

Patients may resist taking medicine and may reject it surreptitiously, failing to realize that they are ill and that it may help them to leave the hospital. Such resistance was inconspicuous in the group using perphenazine, and it was rare for a patient to ask that the drug be discontinued. Most of them accepted it from the very start and seemed willing to continue taking it, presumably because side effects were readily and effectively controlled.

In chronic hospital patients, a change in weight often reflects a change in mental condition. Most patients gain weight when using ataraxics for any length of time, probably because they are able to stay at the table throughout the meal time and can feed themselves adequately. Furthermore, the increased caloric intake is not vitiated and spent by restlessness and hyperactivity. Weight gain in such patients is inevitable, but it is not as noticeable with perphenazine as with other ataraxics. Perhaps it is because sedation is scarcely noticeable that weight gain is at a minimum. On the other hand, the bulimia and

associated gain in weight are attributed by some to be due to a specific metabolic effect of the drug acting on the brain, probably on the hypothalamic area.

Parenteral perphenazine was found to be very rapid in action. Often within 10 minutes of the injection patients became placid, though not oversedated, and most were walking in 30 to 60 minutes. About 3 to 4 ml. (15 to 20 mg.) were injected every four hours for the first few days if patients were too disturbed to take oral medication or refused it. Tablets replaced the parenteral medication in a few days when they became more cooperative and accepted the proffered medication.

Another form used was the liquid concentrate (dram = 16 mg.), diluted, if necessary, to facilitate measuring smaller doses. When uncooperative patients cheeked their tablets and later discarded them, using the liquid form corrected the situation, and in some instances it was mixed with the patient's food without their awareness. The liquid preparation acted more rapidly than the tablets and had the same effect.

Repeated measurements of blood pressure and temperature were recorded all along, and no hypotension or disturbances of temperature were seen. Hyperthermia, reported previously in rare instances with higher doses, was not found in this study even with amounts as high as 360 mg. daily. Tachycardia of 120 was noted in the 4 patients with severe shocklike reactions.

Four lobotomized patients would strike impulsively at others, and occasionally would scream without apparent reason. Such unprovoked, unanticipated behavior is distressing but is not influenced by current treatment methods. It did not respond to the other ataractic drugs, and it was not altered by perphenazine therapy.

SUMMARY

Perphenazine (Trilafon), a new phenothiazine, was used in 363 chronic psychotic women in a large mental hospital. The patients were disturbed and considered treatment failures with other methods used over many years. Functional and organic-type psychoses were studied for 10 months. Four fifths took 32 mg. daily or less; less than three per cent used more than 96 mg. A sixth took the medication less than a month, a fifth more than ten months, and the remainder for varying periods in between. As a rule, improved behavior was seen quite early in the course of treatment. Extrapyramidal symptoms appeared in 38 per cent of those treated, but this rate is inordinately high because the patients were exclusively women. Jaundice was not seen. Hypotension was not evident, nor did depression set in. Sedative effects were not noticed. A severe shocklike state developed in rare instances and could constitute a medical emergency. Senile patients as a rule did not respond to perphenazine as well as younger patients. Most complications responded readily to treatment, without creating resistance in those developing them. A variety of side effects occurred; nevertheless, the over-all clinical impression is that perphenazine is a potent and safe drug even though it was discontinued in 5.5 per cent of the patients. Close medical supervision is necessary for optimum effects and safe administration. Delay in treatment is unfortunate. Although three quarters improved, only some 7 per cent left the hospital because social resources available to the rest had either been exhausted or become

too limited to make extramural placement possible. All community resources must be mobilized and exploited to make maximum use of such treatment programs. Improvement in behavior of large numbers of disturbed patients taking ataraxics creates more favorable living conditions with resultant benefits for all residents on such wards, and the entire hospital treatment program may be improved.

RESUMEN

La perfenazina (Trilafon), una nueva fenotiazina, se empleó en un hospital de enfermos mentales en 363 mujeres con trastornos psicóticos crónicos, que habían sido tratadas por muchos años con otros métodos considerándose el tratamiento un fracaso. Como regla general, se observó mejoría en la conducta muy poco después de iniciado el tratamiento. En el 38 por ciento de las pacientes tratadas se presentaron síntomas extrapiramidales. Esta frecuencia es bastante alta, sobre todo si se considera que los pacientes eran todos mujeres. No se presentó ictericia, hipotensión, depresión ni efectos sedantes. Las pacientes seniles, por lo regular, no respondieron a la perfenazina en igual forma que las más jóvenes. Se observó una variedad de efectos secundarios; sin embargo, la mayoría de ellos respondió rápidamente al tratamiento, sin que se creara resistencia por parte de las enfermas que experimentaron las molestias. La impresión clínica fue que la perfenazina es una droga potente y segura. Es necesaria una extrecha vigilancia médica tanto para administrar el medicamento sin peligro, como para obtener efectos óptimos con la terapéutica.

RESUME

La perphénazine (Trilafon), une nouvelle phénothiazine, a été utilisée dans un grand hôpital pour maladies mentales chez 363 femmes agitées avec psychose chronique, après l'insuccès d'autres méthodes utilisées pendant de nombreuses années. D'une manière générale, l'amélioration du comportement a été observée très précocement au cours du traitement. Des symptômes extrapyramidaux sont apparus dans 38% des cas traités, mais ce taux spécialement élevé est dû au fait que les malades étaient toutes des femmes. L'ictère, l'hypotension, la dépression et les effets de sédation n'ont pas été observés. Les malades séniles n'ont en général pas répondu au traitement aussi favorablement que les plus jeunes. Il s'est produit diverses réactions secondaires, mais la plupart des complications ont cédé rapidement au traitement sans créer de résistance chez celles où elles étaient survenues. L'impression clinique d'ensemble est que la perphénazine est un médicament puissant et inoffensif, mais son administration réclame une étroite surveillance pour obtenir avec sécurité les effets les plus satisfaisants.

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Weight Changes in Relation to the Characteristics of Patients on Chlorpromazine

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During an investigation of behavioral changes occurring on medication with chlorpromazine, data were obtained for the purpose of analyzing the relationship between weight change and certain physical and psychological characteristics.

The sample consists of 59 chronic schizophrenic men patients, characterized predominantly by a long-standing withdrawal and apathy, with an admixture of individuals displaying outbursts of impulsive behavior, anger, or hostility. The mean age is 45.5, with a range of 26 to 69. The mean length of hospitalization has been 14.2 years, with a range of 3 to 32. The group included in the study essentially represents patients who had not been given a regular course of "tranquilizing" medication prior to this investigation, mainly because a good response was not anticipated. Patients who had had psychosurgery and those with a known metabolic disorder or with a physical illness were excluded from the weight investigation. Thirty-three patients were randomly assigned by a disinterested third party to receive chlorpromazine medication and 26 to receive placebo medication.*

Weights were taken weekly by the nursing personnel during a four month period prior to the onset of medication, and during the first two months after the onset of medication. A single weight measure was then taken three months after medication. The dosage throughout this study was 300 mg. daily, divided into three doses.

The relationships between change of weight and changes in behavior (as measured by psychological tasks or tests or by the interview) were analyzed only for those measures on which the chlorpromazine group differed significantly from the placebo group, presumably as a result of the drug. (A full report of the psychological studies will be presented separately.) These measures were the consistency and speed of jump reaction time, and the A and F clusters on the Lorr Interview Scale. Consistency of jump reaction is measured by computing the standard deviation of the 10 reaction time trials at any one sitting; speed of jump reaction is the mean of the 10 trials. The A cluster on the Lorr scale[1] is a bipolar cluster labeled "retarded depression vs. manic excitement" at the low and high ends of the scale, respectively, and is composed of six bipolar items such as mute-overtalkative, restrained-uninhibited, depressed-elated, etc. The F cluster on the Lorr scale is labeled "perceptual distortion" and is composed of five items on which ratings are made for the following behaviors: orientation for people, hostile impulses, hallucinatory experiences, false beliefs. It is assumed to measure the degree of personality disorganization. The behavioral measurements were taken by the investigator (F. H.), who had no knowledge of the prescription code.

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* The placebo tablets were supplied by the courtesy of Smith, Kline & French Laboratories.

RESULTS

During the four month period preceding the onset of medication, no appreciable weight change occurred in either group. Thus the weights of the last week preceding medication were taken as the base values.

During the three months on medication, the patients who were receiving placebo lost weight (an average of 2.5 lb.), whereas patients receiving chlorpromazine maintained their premedication weight with a slight mean gain (1.4 lb.). The analysis of variance[2] is presented in table I. The F (variance ratio) of 4.34 for the AB interaction (expressing the relative change between the two groups) is significant at the 1 per cent level.

The interaction AC in table I evaluates the relationship between the last premedication ("initial") weight and the subsequent weight change. All patients (both on the drug and on the placebo) were divided into three groups according to their initial weight: heavy (170 to 209 lb.), medium (140 to 169), and light (110 to 139). During the three months on medication (either with the drug or placebo), the patients with the high initial weight lost an average of 4.6 lb. and the middle weight group gained 2.8 lb., whereas the low weight group remained unchanged (-0.3 lb.). The F of 5.76 for the AC interaction is significant at the 1 per cent level. The same effect of the initial weight is seen regardless of the drug or placebo medication. Therefore this analysis has separated a source of variability that appears to be independent of the drug effect, namely, the initial weight.

An analysis of variance was also applied to the study of the influence of age upon the weight change. Patients were divided into three groups: old, medium, and young. The chlorpromazine subgroups consisted of 9 individuals each (one hypothetical mean score was added to the young group): old (49 to 69), medium (42 to 48), and young (26 to 41). The placebo subgroups consisted of 11 individuals each: old (47 to 69), medium (40 to 46), and young (33 to 39). The mean weights of the old, medium, and young groups were

TABLE I

Type III Analysis of Variance

Source	Degrees of freedom	Mean square	F
B	1	713.02	1.73
C	2	65,646.20	159.36†
BC	2	71.53	—
Error (between)	54	411.94	
A*	3	28.43	‡
AB	3	40.02	4.34†
AC	6	53.15	5.76†
ABC	6	17.51	1.90
Error (within)	162	9.22	

* A = months, B = medication group, and C = initial weight.

† 1% probability level.

‡ Since the AB and AC interactions are significant, there is no interest in the A main effect.

TABLE II

*Rank-Order Correlations Between Change of Weight and Change on Four Dependent Variables, Computed Separately for Chlorpromazine and Placebo Subjects**

	Chlorpromazine	Placebo
Reaction time		
Variability	−0.46†	−0.03
Mean	−0.24	−0.21
Lorr scale		
A	0.70‡	0.29
F	0.06	−0.05

* The number of subjects for the correlations varies from 20 to 25.
† 5% probability level.
‡ 1% probability level.

144, 160, and 163 lb., respectively. The weights of patients in the "old" groups were significantly lower than the weights in the other two groups (F = 3.32, degrees of freedom = 2/54). Analysis of variance showed no interaction between age and weight changes.

Rank correlation technique was employed to analyze the relationship between changes in the behavioral variables and weight (table II). The only significant correlations occur within the chlorpromazine group. The –0.46 correlation (P = 5 per cent) between weight change and change in variability of reaction time indicates that those subjects who gained more weight also became less variable, i.e., more consistent. The 0.70 correlation (P = 1 per cent) between weight change and change in the A scores of the Lorr scale indicates that those subjects who gained more weight also became more active.

DISCUSSION

It is by now a general clinical experience that patients receiving chlorpromazine usually gain weight, often conspicuously.[3, 4] Moreover, the weight change appears to be associated with behavioral change, since patients gaining the most weight were found to be the ones whose ward behavior, evaluated by the routine nurses' ratings, improved most.[5]

In the present experiment, a conspicuous weight increase had not been anticipated since the behavioral improvement was expected to be moderate on the average, and since the medication period was brief. No observations were made to explain the weight loss in the control group. It may be connected with the decreased food intake in the summer months. Patients on chlorpromazine did not lose weight, and thus, as a corollary interpretation, one may view their weight development as a gain, relative to the control group.

The sample is probably too heterogeneous to allow a study of the relationship between weight gain and age. The lower mean weight of the oldest patients may be a reflection of a general experience, namely, that overweight individuals are rarely found in the highest age brackets.[6]

The interaction between the initial weight and subsequent weight change (independent of

medication) may be of general significance. Evidently the heaviest individuals lost weight. Since there is a correlation between an individual's absolute weight and his fatness,[7] it may be assumed that the heaviest patients were, on the whole, the fattest ones. Thus the weight loss, in this experiment, occurred mainly at the expense of the most obese individuals. Observations made by Garn and Brozek[8] suggest themselves here as pointing toward a similar phenomenon. Their data, derived from a controlled experiment concerned with fat changes occurring on a diet deficient in calories, show that the rate of fat loss in subcutaneous tissue is correlated with the initial thickness of the adipose tissue; it was also found that individuals with initially greater amounts of fat showed greater fat loss. A similar trend can be seen in our experiment. Thus it would seem that more fat is lost where there is more of it.

We suggest that the correlation between change of weight and change on the A factor probably reflects a relationship between improved alertness and weight gain. Although the A cluster is labeled "retarded depression versus manic excitement," in the present sample the scores actually evaluated the degree of alertness, since the sample consisted predominantly of withdrawn, apathetic schizophrenic patients.

Similarly, the correlation of weight changes with the decrease of variability in reaction time can be well understood in terms of the desired drug effect. Individuals who showed a more consistent performance on this test certainly derived benefit from the drug and thus did not lose weight (they felt better, and they ate better).

On the whole, the weight changes observed in this investigation are consistent with an interpretation suggesting that the weight increase usually observed in patients on chlorpromazine is to be attributed at least partly to psychological improvement. Even when the drug is given to patients who show only moderate or minimal signs of anxiety (as assessed by the common observation of ward behavior), the correlation between behavioral and weight changes can be demonstrated. Thus it is seen that change in weight is a useful variable in the study of a drug effect in psychiatric patients.

SUMMARY

During three months' medication with chlorpromazine, a group of chronic schizophrenic patients maintained their premedication weight, whereas a control group lost weight. Heavier patients lost more weight irrespective of medication. Those patients in the chlorpromazine group who gained more weight also became more alert on the A cluster of the Lorr scale and more consistent on a reaction time test. It is suggested that the weight increase is to be attributed at least partly to psychological improvement.

RESUMEN

Durante tres meses de tratamiento con cloropromazina, un grupo de pacientes esquizofrénicos crónicos mantuvo su peso anterior a la medicación, mientras que un grupo testigo perdió peso. Independientemente de la medicación, los enfermos más pesados fueron los que bajaron más de peso. Aquellos otros pacientes del grupo tratado con cloropromazina que aumentaron más de peso se hicieron más alerta según la clase A de la escala de Lorr y re-

accionaron en forma más uniforme a la prueba del tiempo. Se sugiere que el aumento de peso es atribuible, por lo menos parcialmente, a la mejoría psicológica.

RESUME

Durant une cure de trois mois avec la chlorpromazine, un groupe de schizophrènes chroniques ont conservé le poids qu'ils avaient avant la cure alors qu'on observait une perte de poids dans le groupe-témoin. Les malades les plus gros perdaient plus de poids quelle que soit la médication. Les malades du groupe traité par la chlorpromazine chez lesquels l'augmentation pondérale était plus grande étaient aussi plus éveillés, selon la catégorie A de l'échelle de Lorr, et les résultats du test de temps de réaction ont été plus constants. L'auteur estime que l'augmentation de poids doit être attribuée, au moins partiellement, à l'amélioration psychologique.

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International Conference on the Insulin Treatment in Psychiatry

*Charles R. Atwell**

BOSTON, MASSACHUSETTS

On October 24 and 25, 1958, an International Conference on the Insulin Treatment in Psychiatry was held in New York City at the New York Academy of Medicine, under the joint chairmanship of Harold E. Himwich, Galesburg, Ill., Max Rinkel, Massachusetts Mental Health Center, Boston, Mass., and Andrew K. Bernath, of New York City. This conference was sponsored by Dr. D. E. Cameron, Montreal, Canada, Dr. J. S. Gottlieb, of Detroit, Mich., Dr. S. B. Wortis of New York, and the Manfred Sakel Foundation. It was the first such conference after the death of Manfred Sakel in December, 1957.

The purpose of the conference was to assess the value of the insulin shock therapy, after it had been in use for the past 31 years, in the treatment of mental disease, especially schizophrenia. Such assessment had become necessary in view of the number of articles, published in recent years, that seem to indicate that insulin shock has no better effect than other treatments, e.g., prolonged sleep treatment induced by barbiturates; that chlorpromazine and other ataractic drugs have fully replaced insulin treatment; that psychodynamic psychotherapy combined with manipulation of the environment could bring about effects similar to or better than those produced by insulin shock; or that insulin shock was a method of last resort to be used in those cases in which psychodynamic therapy had proved to be a problem. Another aim of the conference was to obtain a global view of the use and distribution of the insulin shock therapy in various countries and continents. Accordingly, a program was prepared comprised of papers on the history of the insulin shock treatment, physiological chemistry of hypoglycemic coma, and clinical-statistical observations.

Experts representing a wide spectrum, from chemistry and neurology to psychoanalysis, including hospital administrators and commissioners of mental health, formed a selected panel whose comments initiated a lively discussion from the floor. The history of the insulin hypoglycemic treatment was brilliantly presented by Joseph Wortis, who, under the direction of Karl M. Bowman, introduced Sakel's shock treatment in this country. Hans Hoff of Vienna, at whose University Clinic in Vienna perhaps the most active insulin unit is in operation, gave a comprehensive report on the history of organic treatment of schizophrenia. The delegate from England, William Sargant, reported comprehensively and critically on the insulin treatment in England and its relation to other physical therapies, and the delegates from South America, Drs. Bermann of Argentina, Pacheco e Silva of Brazil, and Sal y Rosas of Peru, reported on the insulin treatment in their countries. Professor Honorio Delgado, of Lima, Peru, because of reasons beyond his control, could not attend this conference, but he sent a message of good wishes and submitted a scientific paper entitled "Insulin Therapy in Schizophrenia—Our Twenty-Year Experience." Karl M.

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Bowman of San Francisco presented a paper on trends in insulin treatment in psychiatry, and Paul H. Hoch presented one on insulin therapy as compared to drug treatment in psychiatry. Andrew K. Bernath reported his experiences and observations of modification of anxiety subsequent to insulin-induced mild hypoglycemia. Daniel M. Weiss of Boston read a paper on the insulin coma therapy in a Veterans Administration hospital, pointing out reasons why in his hospital the number of patients receiving insulin shock treatment was on the decline, and Karl T. Dussik of Waltham, Mass. (who, at the Metropolitan State Hospital, directs an insulin unit that is the first one aided by a grant of the Manfred Sakel Foundation), reported dynamically on the Sakel's insulin coma treatment in an active treatment unit of today. O. H. Arnold of Vienna, in his paper on the present knowledge about the mechanisms of the effect of insulin treatment, theorized that in schizophrenics prolonged hypoglycemia of the brain leads to the destruction of diseased brain cells, whose function is taken over by normal cells of the same cell family. Ivan F. Bennett, formerly of Washington, D. C., and now with the Research Department of Lilly Chemical, Inc., reported on hormonal and other blood changes occurring during insulin hypoglycemia. Williamina A. Himwich, of Galesburg, Ill., summarized the biochemical changes in the brain during insulin hypoglycemia. Charles A. Sawyer, of Los Angeles, reviewed the electroencephalographic changes in the brain during insulin hypoglycemia, and Samuel Bogoch, of the Massachusetts Mental Health Center in Boston, read a paper on neuraminic acid in the cerebrospinal fluid of schizophrenic patients.

The papers presented provided a commemoration of the work of Manfred Sakel, but, more importantly, they reviewed the whole subject of insulin therapy, drew comparisons between it and other therapies, and presented a world-wide view of the subject. The Austrians and South Americans unanimously agreed that insulin coma is the therapy of choice for schizophrenic reactions of less than two years' duration. The majority of the American workers, however, felt that it should be tried when less complicated methods have failed. The British took the middle of the road course: that insulin coma combined with electric shock therapy in properly selected cases still brings about the most favorable results.

In the discussion, it became even more apparent that, because of the many modifications of the Sakel technique currently in use, a competent and thorough clarification of the Sakel classical therapy has become necessary. In this connection, it was announced at the dinner given by the Manfred Sakel Foundation that the Foundation planned to establish fellowships providing instruction in the original Sakel technique of insulin therapy for schizophrenia. Training centers will be located not only in America but also in Vienna and England.

QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY

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Incorporating the International Record of Psychiatry and Neurology

International Editorial Board

INCORPORATING INTERNATIONAL RECORD OF PSYCHIATRY AND NEUROLOGY

FOREWORD

The purpose of the QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY is to present promptly brief abstracts, noncritical in character, of the more significant articles in the periodical medical literature of Europe and the Americas.

For readier reference, the abstracts are classified under the following general headings:

PSYCHIATRY

1. Administrative Psychiatry and Legal Aspects of Psychiatry
2. Alcoholism and Drug Addiction
3. Biochemical, Endocrinologic, and Metabolic Aspects
4. Clinical Psychiatry
5. Geriatrics
6. Heredity, Eugenics, and Constitution
7. Industrial Psychiatry
8. Psychiatry of Childhood
9. Psychiatry and General Medicine
10. Psychiatric Nursing, Social Work, and Mental Hygiene
11. Psychoanalysis
12. Psychologic Methods
13. Psychopathology
14. Treatment
    a. *General Psychiatric Therapy*
    b. *Drug Therapies*
    c. *Psychotherapy*
    d. *The "Shock" Therapies*

NEUROLOGY

1. Clinical Neurology
2. Anatomy and Physiology of the Nervous System
3. Cerebrospinal Fluid
4. Convulsive Disorders
5. Degenerative Diseases of the Nervous System
6. Diseases and Injuries of the Spinal Cord and Peripheral Nerves
7. Electroencephalography
8. Head Injuries
9. Infectious and Toxic Diseases of the Nervous System
10. Intracranial Tumors
11. Neuropathology
12. Neuroradiology
13. Syphilis of the Nervous System
14. Treatment
15. Book Reviews
16. Notes and Announcements

In fields which are developing as rapidly as are psychiatry and neurology, it is obviously impossible to abstract *all* the articles published—nor would that be desirable, since some of them are of very limited interest or ephemeral in character. The Editorial Board endeavors to select those which appear to make a substantial contribution to psychiatric and neurologic knowledge and which promise to be of some general interest to the readers of the REVIEW. Some articles, highly specialized in character, or concerning a subject already dealt with in an abstract, may be referred to by title only at the end of the respective sections.

A section entitled INTERNATIONAL RECORD OF PSYCHIATRY AND NEUROLOGY is included at the beginning of the journal. The Record Section consists of advanced clinical and experimental reports.

The Psychiatry and Neurology Newsletter was compiled by Dr. Francis N. Waldrop.

The Editorial Board at all times welcomes the suggestions and criticisms of the readers of the REVIEW.

WINFRED OVERHOLSER, M.D.
Editor-in-Chief

Psychiatry and Neurology
NEWSLETTER

CLINICAL NEUROPHARMACOLOGY RESEARCH CENTER: The Clinical Neuropharmacology Research Center, a joint project of the National Institute of Mental Health and Saint Elizabeths Hospital, Washington, D. C., has recently been established at the hospital. Dr. Joel Elkes, formerly Chairman of the Department of Experimental Psychiatry at the University of Birmingham, England, has been appointed chief of the new center and Director of Research for the Hospital. Because of the long-recognized need for the location of basic science and clinical research facilities in a mental hospital setting, an existing clinical service at the Hospital, the William A. White Service, was chosen as the site of the CNRC. It houses approximately 350 psychiatric patients, constituting a representative sample of the hospital population.

Part of the building's ground floor has been remodeled to accommodate some two dozen basic science laboratories in the fields of neurochemistry, neuropharmacology, sensory physiology, neuroendocrinology, electrophysiology, and experimental psychology. In addition, a small modern animal house has been constructed adjacent to the laboratory areas. All laboratories are equipped and furnished according to the standards of the National Institutes of Health. The entire top floor of the building has been adapted to clinical aspects of the research program. It contains a small metabolic ward equipped with a special diet kitchen, laboratories for physiological and biochemical studies, and areas designed for electroencephalographic, psychometric, and psychodynamic studies. This floor also provides administrative office space, facilities for statistical and documentation studies, a library, and a conference room.

Approximately two thirds of the estimated research staff of 60 has been recruited.

Day-to-day planning for the operation of the center is carried on jointly by Dr. Elkes and members of the hospital staff. Clinical personnel assigned to the center by NIMH participate with hospital physicians in the care of patients. Channels of communication between basic science and clinical staff are being developed with the goal of achieving an increasing intimacy of interaction

between the laboratories and the wards as the basis for the natural evolution of interdisciplinary investigation.

Among the activities of the CNRC already under way or in process of implementation is a systematic assessment of the impact of recent pharmacotherapies on the management and treatment of acutely and chronically ill patients, rehabilitation services, staff attitudes and skills, and the changing relationship of the hospital to the community. With the aid of the Biometrics Branch and Socio-environmental Laboratory of the NIMH, close attention is being given to the formulation and calibration of techniques of documentation of objective and subjective changes in patient behavior in ward milieu. Attention is also being devoted to the determination and classification of psychological and somatic responses to pharmacologic intervention in relation to the course of particular illnesses and genetic backgrounds of individual patients. The complex interaction between endocrine and nervous systems, particularly in the context of pharmacological treatment, is being studied. On a more experimental level, studies are being developed to investigate the effects of drugs on the activity of neurohumoral agents within the brain. Psychological studies at the human level will deal with the effects of pharmacological agents upon attention, perception, cognition, sensory discrimination, and learning. Somatic studies will deal with autonomic and fine motor function and the electrical activity of the brain. Such studies will be related to investigations concerning the effects of drugs on the coding of sensory information within the central nervous system of experimental animals. Finally, in other work with experimental animals, studies are being developed to determine the effects of drugs in relation to specific anatomical and biochemical lesions.

AMERICAN BOARD OF MEDICAL HYPNOSIS: The newly established Board of Hypnosis will serve as a certifying body for physicians who make use of medical hypnosis in their professional work. Dr. Jerome Schneck of New York City is President of the new board. Dr. Bernard B. Raginsky of Montreal, Canada, is the Secretary-Treasurer.

AMERICAN GROUP PSYCHOTHERAPY ASSOCIATION REGIONAL MEETING: The fifth annual western regional meeting of the AGPA is scheduled for San Francisco, Calif., April 2 and 3, 1959. Further details may be obtained by writing to Dr. Donald A. Shaskan, VA Mental Hygiene Clinic, 49 Fourth Street, San Francisco 3, Calif.

QUARTERLY REVIEW OF
PSYCHIATRY AND NEUROLOGY

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ABSTRACTS

psychiatry

ALCOHOLISM AND DRUG ADDICTION

1. *Outpatient Treatment of Postalcoholic Syndrome. Response of Two Hundred Forty-Three Alcoholics to Promazine Hydrochloride Given Orally.* HAROLD I. GOLDMAN, Denver, Colo. J. A. M. A. *167*:2069–2071, Aug. 23, 1958.

General hospitals often lack facilities to treat the withdrawal symptoms of acutely exacerbated chronic alcoholism. Treatment of the postalcoholic syndrome thus devolves on the general practitioner, who must cope with such symptoms as severe headache, insomnia, nausea, vomiting, tremulousness, acute hallucinosis, and incontinence of bowels or urine. Past efforts to alleviate or prevent the syndrome in private practice have been largely unsuccessful. The postalcoholic syndrome now is controllable on an outpatient basis. Promazine hydrochloride is recommended, 100 mg. perorally every four hours as required. The drug appears entirely safe for oral administration under the supervision of a private physician; no side effects or complications were noted by the author at the recommended dosage level. Most alcoholic patients sleep within 45 minutes after receiving the first oral dose of promazine. Sleep usually indicates that control of the postalcoholic syndrome is to follow. Patients who respond do so promptly and without intervening delirium tremens. Aggressiveness and boisterousness, so commonly problems in treatment of the acutely inebriated, are completely controlled. The drug apparently affects the vomiting center quickly, for emesis was not observed if the patient retained the tablet as long as 10 minutes. Of 243 outpatients treated, promazine abolished all symptoms in 229 (94 per cent). The drug efficacy indicates that the postalcoholic syndrome can often be alleviated or entirely prevented, which may encourage general hospitals to accept more alcoholic patients even though acutely inebriated or displaying severe abstinence symptoms. The calming influence of promazine should obviate restraints. 6 references.—*Author's abstract.*

CLINICAL PSYCHIATRY

2. *Multidisciplinary Methods in Psychiatric Research.* DAVID MC K. RIOCH, Washington, D. C. Am. J. Orthopsychiat. *28*:467–482, July, 1958.

Certain problems of multidisciplinary research are discussed and illustrated with experience from the Division of Neuropsychiatry, Walter Reed Army Institute of Research, Washington, D. C. It is emphasized that the use of multidisciplinary methods represents a problem in economy and is especially applicable when rare or expensive research material is available. Multidisciplinary projects necessarily vary in structure depending on the degree to which the research areas represented have been systematized. Thus, quite precise design and group collaboration are possible in chemical, physiological, and experimental psychological fields. More exploratory and operational types of projects can be usefully developed in the clinical field. 14 references.—*Author's abstract.*

3. *The Psychiatrist's Responsibilities.* SAMUEL LIEBMAN, MILTON A. DUSHKIN, MARC NISSENSON, AND MARVIN SCHWARZ, Winnetka, Ill. Dis. Nerv. System *19*:332–337, Aŭg., 1958.

Questionnaire data were collected on attitudes and laws related to the psychiatrist's responsibilities when dealing with patients who are homicidal, suicidal, or concerned with dangerous criminal activities. Special problem situations were outlined. In addition, questions were asked about the attitude (legal or implied) and the practice in the community regarding: (1) The confidential relationship between psychiatrist and patient, (2) the mandatory reporting of crime, and (3) suicidal attempts. Subjects comprised a national sampling of psychiatrists, other physicians, attorneys, and social workers. Results indicated that there is lack of uniformity of opinion both between and within the several disciplines, that there is insufficient awareness or misconception of pertinent laws, that fewer than half the states recognize the principle of privileged communication between physician and patient, and that pertinent laws, where present, vary from state to state. Recommendations are made for the establishment of workable principles and policies on a national scale so that professional ethics and appropriate legislation may be developed in harmony with each other. 14 references. 6 tables.—*Author's abstract.*

4. *Language in Schizophrenia. Review of Several Approaches to the Problem.* JOHN PAUL BRADY, Hartford, Conn. Am. J. Psychotherapy *12*:473–487, July, 1958.

Most of what one learns of the psychological functioning of another is by observing his language behavior; by "language" is meant not just the spoken word but also modes of language codification such as gesture and action. This is especially true of the schizophrenic patient, whose use of language reflects the defective state of his ego and his distorted conceptions of himself and the world. The author discusses the subject from three complementary frames of reference: content, the interpersonal situation, and communication theory. Freud, emphasizing the first approach, saw schizophrenic language as a reflection of the regression and narcissism of an ego overwhelmed by instinctual demands. The interpersonal frame of reference is illustrated by the observation that the schizophrenic

patient, overwhelmed by the anxiety of interpersonal relations, fails to use language to establish satisfying contact with others, allowing his language to regress to autism, and hoping to cope with feelings of insecurity by the magical operations he effects with autistic speech. The analysis of schizophrenic language in the framework of communication theory has been particularly rewarding. The author notes, for example, that one develops confidence and skill in the various channels of communication he employs by the assurance he gets from others that he is being understood. When communication is solely one way, as it is when a man broadcasts from the soundproof booth of a radio station (or as it is in the classical psychoanalytic situation), intense anxiety may ensue because the sender has no knowledge as to how his signals are being interpreted. Usually, however, communication is continuously two way and one can modify his own signals (output) in the light of the reactions of others to them (feedback) in order to clarify their meaning and intent (correction). The child whose early communicational experiences are characterized by thwarting and frustration may never develop this facility. He may always feel like the man broadcasting from the soundproof booth—never able to utilize the corrective messages received from others—and his communication may remain essentially one way. The clinical picture of schizophrenia reflects this breakdown in feedback. 34 references.—*Author's abstract.*

5. *Some Problems of Psychiatry in Patients from Alien Cultures.* G. M. CARSTAIRS, London, England. Lancet *1*:1217–1220, June 7, 1958.

Mental disorders occur in every human society, but local material and cultural factors influence both the symptoms that are manifested and the relative frequency of their appearance. This is evident in psychotic illnesses but much more so in neurotic reactions, which can be correctly evaluated only in the context of values and behavior patterns of the societies in which they occur. Examples are given of emotionally conditioned disorders in non-Western cultures, and of their treatment by indigenous healers. A prerequisite for all psychotherapy is the ability to convince the patient that one fully understands his predicament. This can be difficult when patient and therapist belong to different cultures or even to different subcultures within the same society, and yet the therapist's unfamiliarity with his patient's cultural background can be turned to positive advantage if the patient feels that his doctor respects his different values and is interested in learning more about them. Illustrations are given of psychiatric problems presented by patients from overseas and in the proper evaluation of the social background of working class patients in the West. 18 references.—*Author's abstract.*

6. *Dynamic Aspects of Occupational Therapy.* E. A. WITTKOWER AND H. AZIMA, Quebec, Canada. A.M.A. Arch. Neurol. & Psychiat. *79*:706–710, June, 1958.

There is no scientifically valid evidence that work and recreation per se have a remedial effect on the mentally ill, that occupational therapy facilitates the effect of other therapeutic measures, and that the media commonly used are well suited to bring about the desired effects. Objectives of a symptomatic approach to mental illness in the application of occupational therapy are: Habit training, re-education, resocialization, and social remotivation. All these measures have in common a learning process and a disregard for

unconscious mental processes. It is doubtful whether these measures fundamentally affect the disease process as such. A field survey concerning views on and attitudes towards occupational therapy showed that the majority of the patients studied were interested in it but were perplexed about its purpose, that the occupational therapists examined conceived of occupational therapy as a means to direct attention from fantasy and inner preoccupation, to produce a "normal" atmosphere for a "pleasant occupation," and to socialize, and that psychiatrists are likely to regard occupational therapy as a means of breaking the monotony of the day between somatic treatment procedures and meals. Reorientation of occupational therapy with incorporation of dynamic concepts into its usage and with clear definition of its objectives opens up wide possibilities for its application: (1) The main objective of traditional occupational therapy is sublimation. However, the capacity to sublimate has been impaired in, or lost by, the mentally ill. (2) The spontaneously produced objects may serve as a screen on to which fantasies may be projected with their associated drives and defences erected against them. (3) Gratification of originally frustrated infantile needs by appropriate primitive media may lead to progression.

Based on these principles, treatment procedures have been developed: (1) Projective group therapy predominantly suited for psychoneurotic patients, and (2) object relations therapy predominantly suited for psychotic patients. The main feature of the latter procedure was the offering of primitive media, such as mud, brown clay, a baby bottle, and so on. Remarkable improvements from both procedures were observed. 6 references.—*Author's abstract.*

7. *The Performance of Psychiatrists and Psychologists in a Therapeutic Interview.* HANS H. STRUPP, Chapel Hill, N. C. J. Clin. Psychol. *14*:219–226, July, 1958.

This investigation sought empirical evidence on therapists' performance in an initial interview and explored the effects of relevant therapist variables upon: (1) Clinical judgments, including diagnostic and prognostic evaluations; (2) formulations of treatment plans and goals; and (3) communications addressed to the patient. Psychotherapists functioned as vicarious interviewers while viewing a sound film of an initial interview. Data were collected from 235 therapists (psychiatrists, psychologists, and psychiatric social workers). This paper deals with matched samples of 55 psychiatrists and 55 psychologists. The clinical evaluations of psychiatrists were similar to those of psychologists of comparable experience, despite marked intragroup differences. Psychologists as a group seemed to be more passively expectant than psychiatrists. Psychiatrists tended to favor exploratory techniques, whereas psychologists preferred reflections of the patient's feelings. In both groups, clinical evaluations tended to become more unfavorable with increasing experience. Experienced psychiatrists tended to give a larger number of interpretations and showed more initiative. Experienced therapists in both groups tended to be "warmer" in their communications. Therapists' attitudes toward the patient, both among psychiatrists and psychologists, were correlated with certain clinical evaluations, treatment plans, and the emotional tone of their communications. In discussing the implications of these findings, attention is called to the potential effects of interactions between the therapist's emotional reactions to a patient, assessments of the "objective" clinical evidence, and the character of the thera-

peutic interventions; subtle subjective factors in the therapist may influence and color his clinical impressions and adversely affect the resulting character of the therapeutic interaction. 4 references. 4 tables.—*Author's abstract.*

8. *Criteria of Therapeutic Response in Hospitalized Psychiatric Patients.* WILLIAM SCHOFIELD AND PETER F. BRIGGS, Minneapolis, Minn. J. Clin. Psychol. *14*:227–232, July, 1958.

A sample of 100 diagnostically heterogeneous hospitalized psychiatric patients, 61 of whom had received electroconvulsive therapy (ECT), furnished the data for a study of the validity and interrelationships of three measures of Minnesota Multiphasic Personality Inventory (MMPI) profiles, daily nurses' behavior ratings, and clinical evaluation of "condition on discharge." The criterion against which each of these evaluations was checked was occurrence of rehospitalization. Thirty-one per cent of the total sample was rehospitalized. Using the factor of rehospitalization or nonrehospitalization as a criterion to validate immediate posttherapy judgements of patient response, the global clinical judgements had an over-all "hit" rate of 72 per cent and those based on MMPI changes were accurate for 62 per cent of the patients. The clinical appraisals carried a very high rate of false negatives, rating 80 per cent of the rehospitalized patients improved. Predicting rehospitalization or not in terms of concordance of the MMPI judgements and clinical evaluation permitted prediction for only two thirds of the patients, and the over-all increase in per cent of "hits" only slightly exceeded base rate prediction. Behavior ratings based on daily observations of the nursing staff were not reliably associated with the rehospitalized versus nonrehospitalized criterion. The nurses' ratings did demonstrate interesting variation in response of different diagnostic groups to ECT. 5 references. 1 figure. 3 tables.—*Author's abstract.*

9. *The Incidence of Hospitalized Mental Illness Among Religious Sisters in the United States.* SISTER M. WILLIAM KELLEY, Los Angeles, Calif. Am. J. Psychiat. *115*:72–75, July, 1958.

The information of this study was obtained by means of a mailed questionnaire sent to 378 public and private hospitals with psychiatric facilities. Three hundred and fifty-seven hospitals (94.4 per cent) submitted usable responses to the questionnaires, which included questions on present age, age at hospitalization, age at entrance into convent, history of previous hospitalization, and diagnosis. A total of 783 sisters were reported as having been hospitalized for mental illness at some time during 1956. This represented a significant increase over the corresponding rate reported by Moore in 1936. Although incidence of mental disorder is still lower among sisters than among women in the general population, it is increasing more rapidly among the former than among the latter. This increase has been restricted to sisters engaged in active and professional works. The rate of mental illness among cloistered sisters is still considerably higher than among active religious, but the difference between the two groups has decreased greatly since 1936. Among active religious, those engaged in domestic service show a rate of hospitalized mental disorder that is notably greater than among those whose tasks are professional in nature. Functional psychotic

disorders are most numerous in both groups, but they are proportionately more numerous among domestic workers, whereas the less severe psychoneurotic reactions predominate among teachers and nurses. The findings of this study by no means nullify Moore's earlier hypothesis that prepsychotic personalities may be attracted to religious life on the basis of what they think it will be. The apparent increase in mental disorder among active religious, however, suggests that factors of stress may be contributing more to eventual breakdowns than was previously supposed. 6 references. 5 tables.—*Author's abstract.*

10. *Characteristics of Post-Partum Mental Illness.* JOHN J. MADDEN, JOSEPH A. LUHAN, WERNER TUTEUR, AND JOHN F. BIMMERLE, Chicago, Ill. Am. J. Psychiat. *115*:18–24, July, 1958.

The authors studied all cases of mental illness beginning within two months after delivery in patients between the ages of 18 and 40, inclusive, admitted during a four and one-half year period (1947 to 1951), in two psychiatric facilities in neighboring communities; Elgin State Hospital and the psychiatric unit of Loretto Hospital in Chicago. The average bed occupancy during this period at the state hospital was 4500, whereas in the private unit it was only 26; yet there were nearly as many patients (57 versus 59) with postpartum illness cared for in the private psychiatric unit as in the state hospital. The incidence of postpartum mental illness in women between 18 and 40 in the private facility was twice that in the state hospital, 8.9 compared to 4.5 per cent. All the patients in the private hospital unit received electroshock treatment, and a number of the schizophrenic group were treated by means of insulin coma therapy as well. Several voluntary patients with a short-term stay in the state hospital series received no shock therapy. The percentages of lasting good results in schizophrenic, affective, and psychoneurotic reactions, respectively, were 58, 86, and 91 for the private hospital group and 50, 75, and 87 for the state hospital series. However, the duration of hospitalization in the private hospital unit was generally a matter of weeks in contrast to months in the state hospital when the long-term outcome was good. In the authors' experience, the most frequently encountered form of puerperal mental illness of sufficient gravity to require hospital care is the group of schizophrenic reactions. Many of these with a favorable outcome correspond to illnesses that were probably euphemistically and erroneously catalogued in much of the literature of the past three decades as toxic-exhaustive psychoses, and particularly nontoxic deliria. In their beginning, relatively benign postpartum schizophrenic reactions may be very difficult to distinguish from schizophrenia that will progress to deterioration and from those forms with marked tendency to relapse. The proportion of deteriorating and relapsing schizophrenic illnesses is the same whether or not these first developed in the puerperium, implying that process (deteriorating) schizophrenia and some schizoaffective reactions (schizophrenia with manic features) beginning after delivery are purely coincidental psychoses. There seems to be an increasing incidence of serious mental disability of favorable outcome arising in the puerperium that is compatible with psychoneurotic depressive states. About one sixth of the state hospital group of puerperal mental illness and one fourth of the private hospital series were diagnosed as psychoneurotic reactions. In these cases, the psychological stress of motherhood is a potent precipitating and partially causative factor. These reactions occur

in certain women who, when threatened with loss of personality integrity, react with a fairly blatant display of psychoneurotic behavioral symptoms. About half the patients with good long-term recovery from an initial postpartum illness subsequently had one or more children without recurrence. All those in this study classified as having a good outcome have remained well during an observation period averaging more than seven years. With a similar population in the same therapeutic environment, there was found a somewhat better long-term outlook for recovery in puerperal mental illness as contrasted with similarly diagnosed mental reactions unassociated with childbearing. 16 references. 5 tables.—*Author's abstract.*

11. *Toward an Integrated Theory of Schizophrenia.* EMIL G. CONASON AND PERCY E. RYBERG, New York, N. Y. J. Ment. Sc. *104*:372–376, April, 1958.

The authors suggest that the homeostatic mechanisms that operate to maintain sanity in the normal mind are blocked in the psychotic by immunoallergic brain tissue alterations, just as the homeostatic mechanisms regulating somatic tissue metabolism are blocked by such alterations in hay fever, asthma, serum sickness, angioneurotic oedema, contact dermatitis, and other so-called atopic allergic states. Attention is called to the following evidence in support of this theory: (1) The schizophrenic process was successfully reversed in 50 per cent of patients treated by an empirical desensitization procedure described by the authors. (2) Recent publications show that: The sedating effects of the active *Rauwolfia* alkaloids are mediated through the release of serotonin from its binding to brain tissue; asthma, hay fever, and acute rheumatic arthritis are reported to be rarities among populations of mental hospitals as compared to the general population or to nonpsychotic hospital personnel, together with the sharp alternation between asthma (and other so-called psychosomatic illness) and psychosis in some psychotics; recent findings of organ-specific autoantibodies in the blood of patients suffering with Hashimoto's thyroiditis, thyrotoxicosis, and Addison's disease suggest that autoantibodies to nervous tissue be sought in the blood and cerebrospinal fluid of schizophrenics; the tranquilizing effects of an increasing number of drugs of varying chemical structure, such as phenergan, diphenhydramine hydrochloride, chlorpromazine, meclizine hydrochloride, hydroxyzine, and others, may be due to their antiallergic action. 24 references.—*Author's abstract.*

12. *Comparative Effects of Relaxant Drugs on Human Skeletal Muscle Hyperactivity.* FRANCIS A. VASUKA, Phila., Pa. Neurology *8*:446–454, June, 1958.

Clinical observations, motion picture photographic recordings, and electromyographic and myometric studies were performed on 11 individuals with neuromuscular disorders prior to, during, and following the oral administration of 1250 mg. of methocarbamol given four times a day, 500 mg. of meprobamate given three or four times a day, and 500 mg. of zoxazolamine given three or four times a day. Alterations were noted on spasticity, ankle clonus, clonic extensor spasms, flexor spasms, and functional capacity as manifested by self-care and ambulation abilities. The variations were recorded when each subject received the three drugs in series. Each modality of muscle hyperactivity was not depressed to parallel levels. The major benefit derived by the 11 patients was a partial alleviation of

muscle hyperreactivity, which in turn allowed for greater self-care capabilities and easier ambulatory capabilities. Urinary frequency was lessened. Wheel chair patients could sit more comfortably and manipulate the chair without aid. Movements no longer threw their extremities into severe clonic extensor spasms. The present study indicates that meprobamate in the dosage noted was more effective than zoxazolamine and methocarbamol as a muscle relaxant in the human. The dosage of methocarbamol described was found to be more effective in relieving muscle spasticity than that of zoxazolamine. 16 references. 6 figures. 2 tables.—*Author's abstract.*

HEREDITY, EUGENICS, AND CONSTITUTION

13. *An Appraisal of Psychogenic Twin Data.* FRANZ J. KALLMANN, New York, N. Y. Dis. Nerv. System *19*:9–15, July, 1958.

No general theory of human behavior nor causal model of specific abnormal behavior patterns can be construed in a genetic vacuum, without some reference to primary gene action. Ethnoplastic experiences that mold personality, and the formative elements that secure moldability on the human level, are end products of the same evolutionary process and, like both sides of a coin, defy separation into independent variables. The twin study method has made it possible to amass a wealth of empirical data on the interaction of genetic and nongenetic factors in normal and pathological behavior variations. In various areas, however, there is still an emphatic need for well-planned cross-sectional and longitudinal twin data. Reluctance to recognize the operation of genetic elements in the etiology of such psychoses as schizophrenia and manic-depressive psychosis is certain to have harmful consequences in a number of respects. Apart from omissions in treatment and family guidance, damage may be caused by disregard of two general genetic phenomena: (1) The hazards of a gradual increase in the number of poorly adapted carriers with a chance of reproduction, such as may result from assortative mating trends and improved medical techniques; and (2) further increases in the mutation rate of populations due to excessive use of ionizing radiation. In a psychiatric-genetic program of general public health measures, the foresight implicit in a concern with the health of future generations is needed as urgently as is increased genetic knowledge. 24 references.—*Author's abstract.*

PSYCHIATRY OF CHILDHOOD

14. *Childhood Schizophrenia: A Review.* JAY KUTEN AND SANDRA L. KUTEN, St. Louis, Mo. Dis. Nerv. System *19*:253–260, June, 1958.

The literature of childhood schizophrenia is a confusing one. The basic ideas about the disorder are still debatable, and the many different classifications of the disease have done little to solve the fundamental problems of diagnosis, etiology, and pathogenesis. This review attempts to impose order by viewing the disease in the perspective of cultural influences on our thinking. Language emerges as one of the greatest barriers to progress. There is no standard nomenclature describing schizophrenic children. Every author is forced to develop his own descriptive terms and diagnostic criteria to fit those terms. Furthermore, clinical studies are lacking in statistical evaluation, and, therefore, epidemiological

information cannot always be accepted as valid and generally applicable. But the diversity of terminology contrasts with uniformity of description of the childrens' bizarre motor activity, seclusiveness, and lack of effective awareness of other human beings. The essence of this agreement in the literature has been summarized in the idea that the basic process of childhood schizophrenia is the child's inability to distinguish the boundary of his body from that of the environment. One theory has been chosen that explains this inability of schizophrenic children to properly distinguish between self and the outside world on the basis of biological consideration of human development. This work, that of Yakovlev, suggests the cortical association areas as the neuroanatomical site of the underlying pathology. Although concepts of etiology and pathogenesis must remain speculative where diagnosis is still so uncertain, these ideas of Yakovlev represent an original contribution to thought. Further progress depends on the solution of the semantic problems, consideration of biology, accurate clinical study, and the use of statistics as an evaluative tool. 53 references.—*Author's abstract.*

PSYCHIATRY AND GENERAL MEDICINE

15. *Predictive Psychophysiological Studies.* E. D. WITTKOWER, Montreal, Canada. Acta psychotherap., psychosom., et orthopaed. *6*:11–22, 1958.

Three predictive psychophysiological studies concerning ovarian, thyroid, and gastric function are reported. It has been possible to verify some aspects of psychoanalytical theory by rigorously designed experimental procedures. Predictive psychological changes related to ovarian function have been demonstrated. Application of psychodynamic criteria established on examination of thyrotoxic patients to neurotic patients allows prediction of their rate of thyroid secretion with reasonable accuracy. Similarly, on the basis of psychodynamic criteria, gastric hypersecretors could be differentiated from gastric hyposecretors by psychological tests. An attempt was made to predict on a basis of test results which army draftees would develop duodenal ulcers during 16 weeks of basic training. Of 10 men selected, the prediction was correct in seven. 19 references.—*Author's abstract.*

PSYCHIATRIC NURSING, SOCIAL WORK, AND MENTAL HYGIENE

16. *Post-Hospital Adjustment of Chronic Mental Patients.* G. W. BROWN, G. M. CARSTAIRS, AND GILLIAN TOPPING, London, England. Lancet *2*:685–689, Sept. 27, 1958.

A follow-up inquiry was completed for 229 (95 per cent) of 240 male patients discharged after more than two years' stay in seven mental hospitals in the London area. All were subjects of the United Kingdom, aged 20 to 65 on discharge, and were not known to have gone to an address outside London. Sixty-eight per cent of the patients succeeded in remaining out of the hospital for at least a year. Sixty-six per cent of these were rated as having full or partial adjustment at the end of the year, as measured by: (1) Employment, (2) ability to look after themselves with regard to personal appearance and use of money, and (3) showing adequate interpersonal relationships. In this group of patients, the outcome bore little relation to the patient's age, recorded diagnosis, or length of stay in hospital.

Relapse was shown to be associated with clinical state on discharge, with subsequent employment, and with the social group to which they went: patients staying with siblings or in lodgings did better than those staying with parents, with wives, or in large hostels. This result was particularly clear for schizophrenic patients, who formed 68 per cent of the total. Schizophrenic patients appeared to fare worst in situations where they were obliged to enter into close personal relationships with other members of the household. Employment was especially strongly associated with survival in the community for schizophrenic patients: relatively more nonschizophrenic than schizophrenic patients were supported by their relatives although they remained unemployed. The social liability presented by these chronic patients to their households and the need for supportive social work with expatients and their families were discussed. 11 references. 5 tables.—*Author's abstract.*

PSYCHOANALYSIS

17. *Psychoanalytic Applications to Levels of Group Psychotherapy with Adults.* BENJAMIN KOTKOV, Brattleboro, Vt. Dis. Nerv. System *19*:379–385, Sept., 1958.

The practice of group psychotherapy, a review of the literature, and experimental work on goals disclose three distinct levels of psychotherapeutic achievement in group psychotherapy: (1) Social participation, based chiefly on symptom identification; (2) increased confidence, based chiefly upon ego identification; (3) emotional insight, based chiefly upon modified superego identification. The purpose of this paper is to point out the similarity in dynamics for all psychotherapeutic echelons as well as to enumerate the special characteristics unique for each. The commonalities lie with the basic core applicable to all analytically oriented group psychotherapies with adults regardless of nosological syndromes, age, intelligence, or presenting complaint, namely, reactions of patients to the group situation, the psychotherapist's noninterventionalist role, and use of patients as adjunct therapists. However, the characteristic defenses, the use of repression, the tempo and progress, and the standards of goals achievable will vary with the type of group. The group ego may be loose, rigid, or encouragingly flexible. Correspondingly, three psychotherapeutic levels are described in this paper, leading to social participation, increased confidence, and emotional insight. 50 references.—*Author's abstract.*

18. *A Comparison of Psychoanalysis with the Dynamic Psychotherapies.* WILLIAM F. MURPHY, Boston, Mass. J. Nerv. & Ment. Dis. *126*:441–450, May, 1958.

There are theoretical and technical differences between classical psychoanalysis and the majority of the dynamic psychotherapies. The possibility of confusion between the two has been enhanced by modifications of the analytic technique for the purpose of treating borderline psychotics and other difficult cases, and by the vagueness, lack of a clinically well-substantiated theory, and general looseness of technique on the part of the dynamic psychotherapies. In all procedures, the patient is encouraged to talk freely and the therapist tries to obtain some holistic perspective and understanding of the origin, development, and meaning of the patient's symptoms and difficulties and to communicate his knowledge to the patient. How this is done depends upon theoretical premises and schemata concerning

the nature of mental illness. The process of psychoanalysis is accompanied by characterological changes in the patient that make him capable of an optimal adaptation to reality. Any of the technical elements in psychoanalysis may be used in the dynamic psychotherapies, but there is little or no consistency in the approach. In the psychotherapies, mainly because of the uncertainty of the role and the technique, the therapist is more active verbally and pays more attention to the manifest content of the patient's speech; the analyst, more to the unconscious import of his words. In psychotherapies, the transference relationship is undeveloped and complicated by the reality relationship. Psychoanalysis teaches that symptoms of the neurotic and the psychotic are the logical end result of a pathological way of life. It will be of great interest to observe the complications that may arise and are inherent in the modification of acute symptoms by chemical means, especially in cases of psychosomatic illness. As far as obvious results are concerned, there is little to choose among any of the dynamic psychotherapies. 28 references.—*Author's abstract.*

TREATMENT

a. General Psychiatric Therapy

19. *Management of the Paranoid Schizophrenic with Psychotherapy.* MAXWELL BOVERMAN, Washington, D. C. M. Ann. District of Columbia *27*:231–237, May, 1958.

Uncritical enthusiasm of the tranquilizers has obscured the viewpoint that schizophrenia is a disease of personal relationships and is capable of being approached psychotherapeutically. Some critical factors and their significance in the developmental history of the paranoid patient are discussed, and some psychological forces involved in the personal interplay leading to the psychosis are presented. Several cases in which the paranoid psychosis was approached exclusively by psychotherapy are given. A therapeutic approach requires certain modifications of psychoanalytic technique. In general, these have to do with the necessity for activity on the part of the therapist, specifically in the following areas: firmness, reality confrontation without equivocation, insistence that reality demands (work and responsibility) be met, interpretation of (rather than satisfaction of) infantile hostility and helplessness, use of significant members of the family as adjuncts to treatment, and the avoidance of hospitalization or other escape situations for therapy. The psychotherapeutic approach to the paranoid psychosis can result in improvement not only in terms of superficial clinical or symptomatic nature but also in actual personality change with the formation of more effective and adult ways of dealing with human relationships. This paper questions the concept of schizophrenia's being impervious to dynamic understanding or the psychotherapeutic approach and, by theory and example, shows that such an approach is possible and merits further interest and study. 2 references.—*Author's abstract.*

20. *Psychotherapy with Ambulatory Schizophrenic Patients in Mixed Analytic Groups.* WILFRED C. HULSE, New York, N. Y. A.M.A. Arch. Neurol. & Psychiat. *79*:681–687, June, 1958.

A new group psychotherapeutic method for the treatment of schizophrenic patients is described. The majority of schizophrenic patients eligible for this type of therapy belong

to the not actively psychotic categories, i.e., they are mostly prepsychotic patients whose disorders were diagnosed as so-called borderline states, pseudoneurotic schizophrenia, simple schizophrenia, latent schizophrenia, or schizophrenic character disorders. In a few instances, psychotic patients with delusional and hallucinatory states were admitted and responded well. The paper reports on the application of psychoanalytically oriented group psychotherapy to ambulatory adult schizophrenic patients. The groups are organized in the private psychiatric office or in hospital outpatient clinics. The therapeutic group is composed of 6 to 9 carefully selected patients of either sex or both sexes; the majority of the patients are suffering from psychoneurosis or character neurosis. Only a very small number of patients (1 or 2) with schizophrenia are admitted to each group. Groups meet once or twice weekly for 90 to 100 minutes. The majority of the patients receive group psychotherapy exclusively, but provisions for concomitant individual therapeutic sessions are made. This type of psychotherapy can, and often has to, be applied continuously over one or several years, even if the composition of the group changes during the treatment period of a specific patient. Case material shows that the majority of the patients selected for this kind of therapeutic approach responded well and showed decrease of depressive and fearful feelings, greater closeness to reality, increased social activity and responsibility, and improved interpersonal relations. A certain percentage of failure, even among carefully selected patients, is reported. An attempt is made to clarify the psychodynamics of this therapeutic approach and to show the actual contributions that the schizophrenic patients can make to the treatment of the neurotic group members. 10 references.—*Author's abstract.*

21. *Factors Affecting Results in Psychotherapy.* JEROME A. OREMLAND, DON D. JACKSON, GEORGE KRIEGER, AND ROBERT BLAZEJACK, Palo Alto, Calif. Dis. Nerv. System *19*: 289–294, July, 1958.

Eighteen male patients from the disturbed unit of the Veterans Hospital who were treated primarily with psychotherapy were studied approximately four years after admission. Each was rated on developing insight, improving judgment, better control of feelings, and increasing ability to relate. A patient rated as improved (44 per cent) showed improvement in at least three of the spheres, and one rated as unimproved (56 per cent) showed little improvement in two or more spheres. At the end date, 2 patients were discharged and well, 5 were discharged with uncertain whereabouts, 6 were privileged in our hospital, 1 was not privileged in our hospital, and 4 were in other mental hospitals. Follow-up shows that there was a continuum of prognosis for psychotherapy with depressive reaction at the good end, character disorders at the poor end, and neurotic and schizophrenic group in between. Comparison of the improved-unimproved groups shows that a patient admitted as intoxicated, regardless of diagnosis, did not respond. Psychotherapy was relatively successful for depression or suicidal symptoms, whereas patients with confusion did not respond. The assaultive patients were nearly equally distributed in the two groups. Shorter lapse of time between first symptom and initiation of therapy was related to improvement, whereas many previous hospitalizations were not. The improved group was strikingly free of divorced men. Higher military rank was related to improvement especially when length of

service was short. Compensation did not mitigate against motivation. The unimproved group had a greater proportion who had had previous somatic therapy. It was shown that the longer the patient was in therapy and the more experienced his therapist the better his chance for improvement, even though he had had more than one therapist, and that therapy-unsupervised patients tended to make greater gains than therapy-supervised patients, suggesting that the therapist's relationship to a supervisor may act as an anti-therapeutic factor. With regard to subsequent somatic therapy, including tranquilizers, of the 9 patients who were so treated only 3 showed improvement. 9 references. 15 tables. —*Author's abstract.*

22. *Psychotherapeutic Aspects of Male Homosexuality.* L. H. RUBINSTEIN, London, England. Brit. J. M. Psychol. *31*(1):14–18, 1958.

Many cases of homosexuality can be accurately described as monosymptomatic phobias, in which peace of mind is maintained so long as the danger situation, namely, sexual contact with women, is avoided. Mostly, however, the unconscious anxieties are hidden by attitudes of superiority and hate or, the reverse, by exceptional ease in social contacts with women. Moreover, the still-prevalent tendency to overstress the importance of constitutional factors helps to hide the neurosis. Psychotherapy should, in the first place, be offered to those homosexuals who are already aware of some psychological disturbance. In view of the limited facilities for dynamic psychotherapy, the therapist must often content himself with an exploration of the more obvious causal and contributory factors. The resulting better understanding and reduction of some of the irrational guilt and anxiety can benefit society as well as the individual. This will not turn an unhappy homosexual into a happy one; the idea of the "happy homosexual" is very much of a myth. The selection of patients for more radical treatment by psychoanalysis, or at least psychoanalytically oriented psychotherapy, presents difficult problems. One should not be too rigidly guided by considerations of age. Apart from the young homosexual of the "late developer" type, the age group between 20 and 30 is generally the more amenable one, but good results can occasionally be obtained with homosexuals between 30 and 40. It is equally important not to distinguish too sharply between active and passive homosexuals since the two attitudes are often closely intermingled. The most important prognostic criterion is the strength and depth of the homosexual's feminine identification. It is no easy task to distinguish the homosexual whose condition is mainly determined by edipal conflicts from the homosexual whose problems are rooted in a severe pre-edipal disturbance. The relative significance of disturbances at the various levels may in certain cases be gauged from the history, and more accurately from the evaluation of other symptoms relating to particular stages. Classification according to the Kinsley rating scale can give useful prognostic indications, but it is limited to conscious experience. An exploratory analysis is the best means for diagnosis in depth rather than by surface signs. To sum up the conclusions from ten years' experience of treating overt homosexuals: A fair number can be helped to a certain extent; some can improve well beyond original expectations. Complete psychoanalysis remains the treatment of choice; but modified forms of analysis can achieve satisfactory results in well-selected cases.—*Author's abstract.*

b. Drug Therapies

23. *Sodium Amytal and Extraversion.* S. G. LAVERTY, Edinburgh, Scotland. J. Neurol., Neurosurg. & Psychiat. *21*:50–54, Feb., 1958.

Sodium amytal and placebo injections were given to 40 subjects divided into four groups of 10: neurotics, normals, introverts, and extraverts. Scores on the Guilford R scale (extraversion) were higher after amytal than after placebo injection. This increase was significant for the introverted neurotic group but not for the other groups taken individually. Changes in reported symptomatology were noted after amytal injection; these included an increase in the quantity of recorded spontaneous talk and a reduction in reported anxiety, depression, recurrent thoughts, and other symptoms. Hysterical symptoms were unrelieved in 5 but relieved in 2. The point at which speech became slurred during amytal injection was difficult to assess, but it appeared to occur earlier in extraverted subjects. It is suggested that sodium amytal produces a behavioral shift towards extraverted behavior at a point before drowsiness and sleep are induced, and reduces the restriction of outward expression seen in introverted subjects. This shift is compared with the shift in electroencephalographic response to peripheral stimulation during barbiturate anesthesia described by Brazier and attributed to depression of a subcortical "inhibitory system." 13 references.—*Author's abstract.*

24. *Clinical and Laboratory Observations on LSD-25.* MYRON FIELD, JOSEPH R. GOODMAN, AND JOHN A. GUIDO, Long Beach, Calif. J. Nerv. & Ment. Dis. *126*:176–183, Feb., 1958.

Clinical and laboratory techniques were used in an attempt to find some practical utilization of LSD-25. Three types of patients were used in the study. The diagnostic categories were obsessive-compulsive, chronic brain syndrome, and "obsessiveness" (a nonstandard diagnosis utilized to describe patients who are chronic symptom complainers). A standard 100 μg. dose of LSD-25 was given each patient. With the obsessive-compulsive patient, breaking of the obsessive-compulsive cycle was attempted at the height of the effect of the drug. This might be thought of as reconditioning. In the "obsessiveness" patients, the Rosen interpretive technique was utilized with full use of the strong transference typically made by patients under LSD-25. In patients with organic disorder, no significant therapeutic effects were observed. The obsessive-compulsive patients improved. The most success was obtained with patients in the "obsessiveness" category. Laboratory tests were run in an attempt to evaluate the mechanism of action. Eosinophil counts were used to observe the effects of LSD-25, adrenalin, and ACTH. It was found, on repeated use of LSD-25, that there was not only a block in the clinical manifestations of the toxicity but also a correlated failure to produce a drop in eosinophils. At this point, 0.5 ml. of adrenalin also failed to produce a drop in eosinophils whereas ACTH still produced this response. This strongly suggests that the block takes place at the hypothalamic-pituitary level rather than at the adrenal cortex. Further correlations were found between the type of hallucinations described by some patients to whom LSD-25 had been administered and those of 2 patients with hypothalamic syndromes, manifested by severe hyperthermia,

diabetes insipidus, and gastric ulcer, to whom it had not. The hallucinations described by the latter two patients were almost identical with those elicited by LSD-25. 15 references. —*Author's abstract.*

25. *Some Pharmacologic Correlations of the Chemotherapy of Mental Disease.* EDWARD B. TRUITT, JR., Baltimore, Md. J. Nerv. & Ment. Dis. *126*:184–210, Feb., 1958.

The pharmacologic agents for the treatment of mental disease are classified in this review under three divisions: depressive reactions, schizophrenic reactions, and psychoneurotic reactions. For depressive reactions drugs were divided into stimulant drugs, such as iproniazid, pipradrol, and methylphenidate, and pharmacoconvulsive agents, such as hexafluorodiethyl ether, pentylenetetrazole, hexazole, and thiocarbohydrazide. Reserpine and other *Rauwolfia* derivatives and phenothiazine derivatives, such as chlorpromazine, are discussed as to their role in the treatment of the schizophrenic reactions and their mechanism of action. An exception is taken to the hypothesis that reserpine exerts its central sedative action through the action of serotonin liberation. Evidence favoring the concept of central depletion of serotonin as its mechanism of action is compiled. The principal drugs reviewed for treatment of psychoneurotic reactions include meprobamate, benactyzine, phenaglycodol, and various sedative antihistaminic drugs such as hydroxyzine, phentoloxamine, and doxylamine. The pharmacologic similarity of meprobamate to mephenesin, trimethadione, and various barbiturates is discussed in relation to its mechanism of action. The general conclusions are drawn that: (1) Mental depression may be related to either a neurohumoral deficiency of cerebral serotonin or some sympathomimetic amine or to an enzyme disorder such as a monoamine oxidase overactivity in the adrenergic excitatory mechanisms of the brain that might produce such a deficiency; (2) drugs that are most effective in curbing the acute mania, motor excitement, and hallucinations of the schizophrenic reaction are those that interfere in some manner with the adrenergic excitatory centers for the emotional responses in the brain as exemplified by reserpine and chlorpromazine; (3) psychoneurotic symptoms respond most favorably to drugs that have a minimum of side effects and produce a relaxation of neuromuscular tension and anxiety with a minimum of drowsiness and other symptoms of central nervous system depression. 297 references. 2 figures. 2 tables.—*Author's abstract.*

26. *A Controlled Trial of Methyl Phenidate (Ritalin) in the Treatment of Depressive States.* A. A. ROBIN AND S. WISEBERG, Essex, England. J. Neurol., Neurosurg. & Psychiat. *21*:55–57, Feb., 1958.

A double-blind controlled trial of methyl phenidate (Ritalin) was undertaken on 45 patients. Two groups (22 drug-treated cases and 23 control patients) were shown to correspond in their sex distribution, age, civil state, personality types precipitating factors, duration of illness, type of treatment given previously and concurrently, intelligence as measured by the Kent oral test, prognosis as estimated by the psychiatrist, and depth of depression as measured by a modification of the Minnesota Multiphasic Personality Inventory (MMPI)) devised by the authors.

Two patients abandoned the drug because of unpleasant side effects, and 3 patients failed

to complete the month's treatment period. For the remaining 40 patients methyl phenidate in doses of 10 to 20 mg. twice a day was shown to have no advantage over a placebo in the treatment of depression or associated symptoms. No increase in the rate of performance was demonstrated with the drug. It was felt that the Kent oral test, the modified MMPI, and a modification of the Porteus mazes, as used for the trial, all quickly performed tests, may have value in standardizing results of outpatient studies. 9 references. 2 tables.—*Author's abstract.*

27. *Use of Reserpine on a Chronic Disturbed Ward.* HARRY ADLER, Los Angeles, Calif. Internat. Rec. Med. *171*:83–86, Feb., 1958.

In a study, 143 patients in a chronic disturbed ward were treated with reserpine. The dosage varied from 4 to 20 mg./day, with 5 mg. as the most frequent dosage. There were 117 schizophrenics, and the remainder were manic depressive, character disorder, and organic type illness. Assaultiveness, hyperactivity, and accidents decreased, and there was far less need for all form of restraints. Because of the less tense atmosphere patients were less frightened, seclusive, and withdrawn. Patients were more friendly and cooperative and more active in all group activities. Patients with anxiety, insecurity, grandiosity, and hyperactivity responded well, whereas patients with character disorders did poorest. Anxiety is definitely lacking in patients with character disorders; they react with basic or primitive emotions. Patients with somatic symptoms responded poorly because the somatic displacement was a necessary defense. Hyoscine, barbiturates, and electroshock therapy were each combined with reserpine; the reserpine-electroshock therapy combination produced the best results. Side reactions such as psychomotor trembling and tension evoke fear and hostile reactions and require prompt aid by use of sedatives, Artane, or reassurance. Ideas and feelings that are disturbing erupt under reserpine therapy, and the more the patient learns to cope with them the better the prognosis. Treatment must be prolonged in the hospital and at home in spite of side reactions. 11 references. 2 tables.—*Author's abstract.*

28. *Studies in the Effect of Lysergic Acid Diethylamide (LSD-25). Self- and Object-Size Perception in Schizophrenics and Normal Adults.* ROBERT S. LIEBERT, H. WERNER, AND S. WAPNER, Worcester, Mass. A. M. A. Arch. Neurol. & Psychiat. *79*:580–584, May, 1958.

Under the influence of lysergic acid diethylamide (LSD-25), for both normal subjects and schizophrenic patients there is a significant increase in the perceived size of one's own body and its parts and no significant change in the perceived size of external objects. These findings are interpreted in terms of the assumption that LSD operates as a primitivizing agent, which is assumed to lessen the definiteness of the boundary of the body in relation to the surroundings. 5 references. 3 tables.—*Author's abstract.*

29. *High Dosage Compazine in Chronic Schizophrenia.* W. T. HOLMAN, Benton, Ark. Dis. Nerv. System *19*:309–310, July, 1958.

Thirty patients with chronic schizophrenia who had not responded to other methods of treatment were treated with relatively high doses of prochlorperazine (Compazine), without

benefit of conventional adjunctive therapy, with remission being achieved in 17 of the 30 (56.6 per cent) after three months. No serious side effects were encountered. Although extrapyramidal signs occurred, they were readily controlled with adjunctive Artane, which did not necessitate reduction of dosage of prochlorperazine. Further, extrapyramidal signs from phenothiazine derivatives appear to indicate high therapeutic activity. The antiemetic action of prochlorperazine necessitates close observation of patients receiving high doses, since it may mask intestinal obstruction or brain tumor. Although no clinical evidence has been reported, the frequency of extrapyramidal signs occurring with prochlorperazine therapy raises the question as to its contraindication in lesions of the basal ganglia. Prochlorperazine appears to have advantages over other phrenotropic drugs in the treatment of chronic schizophrenia, but, like any other therapeutic agent, it must stand the test of time. 4 references.—*Author's abstract.*

30. *Glucose and Insulin in Schizophrenia.* SHEILA R. LEYTON, Worcestershire, England. Lancet *1*:1253–1254, June 14, 1958.

Since no one had compared the effect of insulin hypoglycemia and glucose with the effect of glucose alone in the treatment of schizophrenia, a small investigation was undertaken in the Insulin Unit at Powick Hospital by dividing all patients referred to the Unit alternately into two groups of 15 patients each, one of which received standard insulin and the other glucose alone. The insulin treatment was given along customary lines, termination of hypoglycemia being by intravenous injection. The fasting glucose patients were given injections of sterile water at the same time as the insulin was given. While the patients receiving insulin were in coma, those receiving glucose were kept in bed and, to occupy them, asked to write on selected subjects. For the first week the patients receiving glucose were given a sugar drink at the same time as those who were receiving insulin and who were in the precoma stage. In the second week they received 20 ml. of intravenous glucose followed by the drink, in the third week 40 ml., and in the fourth week 60 ml. From 40 to 50 injections were given, in all comparable to the 40 comas of the patients receiving insulin. Exactly the same attention was paid to both groups of patients with regard to talks and visits by the medical officers, diet, occupational therapy, and so on. No sedatives were administered at night. The average age of the patients receiving insulin was 25 years and of the patients receiving glucose 26. The results were assessed by whether the patients were discharged from hospital or not. Of the 15 patients in each group, 7 of each group were discharged from hospital.—*Author's abstract.*

31. *Psychodynamic Drugs. (A Re-evaluation and Report).* RICHARD C. PROCTOR, Winston-Salem, N. C. Dis. Nerv. System *19*:265–268, June, 1958.

This paper is concerned with a word of caution on the use of so called tranquilizing drugs in the handling of emotionally disturbed patients, but at the same time it points out the great value these drugs have when properly utilized. It also contains a report on three newer drugs that have been used by the author. The first is Nicozol with reserpine, a combination of nicotinic acid, pentylenetetrazol, and reserpine. The drug appears to be beneficial in the handling of elderly patients with psychiatric symptoms; 65 to 70 per cent of the patients show a mild to marked improvement, with no untoward side effects.

The second drug is liothyronine (Cytomel), which has been available for about three years for the treatment of hypothyroidism. A group of 30 patients with depressive reactions were treated with a dosage of from 15 to 50 μg./day. Seventeen patients showed an improvement that was marked enough to be obvious to the patients themselves as well as to their families and friends. The third drug is Quiactine, which was given to nearly 100 patients on an outpatient basis. Half of these patients were treated in an industrial setting at the Hanes Hosiery Mills Company in Winston-Salem, N. C., for anxiety, tension headaches, backaches, agitation, and restlessness. Between 60 and 75 per cent of the patients treated with this drug showed clinical improvement that became apparent within one week after therapy began. It has proved useful to patients working around machinery, and those who drive automobiles or trucks, because of its minimum sedative effect. 17 references.—*Author's abstract.*

d. The "Shock" Therapies

32. *Clinical Correlates of Electroshock Therapy.* ROBERT B. AIRD, San Francisco, Calif. A.M.A. Arch. Neurol. & Psychiat. *79*:633–639, June, 1958.

Previous studies, which showed that the permeability of the blood-brain barrier was markedly increased by a series of electrically induced convulsions, were reviewed in the light of possible correlations with the clinical effects of electroshock therapy. That the physiologic effect of convulsive phenomena responsible for the therapeutic effects of electroshock may lie in cerebrovascular permeability changes, as demonstrated in the studies reviewed, was suggested by the following considerations: (1) Cerebrovascular permeability constitutes a basic neurophysiologic mechanism capable of conditioning the neurophysiology of the central nervous system; (2) as demonstrated, this mechanism may be modified over relatively prolonged periods by electrically induced convulsions, and hence might produce neurophysiologic effects that could be correlated with the somewhat sustained clinical benefits of electroshock therapy; and (3) although neurophysiologic processes, directly or primarily involving neuronal elements and pathways, could scarcely be expected, from what is known of them, to produce persistent effects, the mechanism considered has the advantage of offering an explanation for a sustained conditioning of these elements without itself being dependent upon them. Further evidence was adduced which suggested that the primary action of electrically induced convulsions was cortical rather than subcortical in location, and that they may act to condition the cortex neurophysiologically so as to heighten its inhibitory action. If, as has been postulated, the therapeutic effectiveness of shock treatment depends upon the modification of behavioral patterns by hypothalamocortical interaction, the cortical effect of increased cerebrovascular permeability offers an attractive hypothesis that would explain the prolonged neurophysiologic effect of electroshock without implication of a primary neurogenic action. A similar effect at deeper, diencephalic levels is not precluded by this concept, and a final comprehensive formulation of the neurophysiologic basis of electroshock was suggested that involves the conditioning of both cortical and deeper components by persistent cerebrovascular permeability changes. 43 references. 1 figure. 1 table.—*Author's abstract.*

neurology

CLINICAL NEUROLOGY

33. *The Nature of Apraxia.* D. DENNY-BROWN, Boston, Mass. J. Nerv. & Ment. Dis. *126*:9–32, Jan., 1958.

The author presents a critical discussion of disorders of movement without paralysis resulting from cerebral lesions, commonly classified as apraxia. The most complex type of difficulty relates to propositional or mimetic performance, for example, pretending to drink from a glass of water. This type of disorder is ideational apraxia and is associated with the perceptive defect of agnosia and corresponding lesion of the dominant hemisphere. The author holds that perseverating motor performance in relation to certain specific classes of object is a minor degree of the same ideational defect. Loss of abilities requiring a leading hand for their natural performance is a special type of ideational apraxia for which the underlying perceptual defect is probably the same as for constructional apraxia. He favors abolition of the confusing term ideomotor, often applied to these types of disorder. The part played by lesion of the corpus collosum in such "ideomotor" apraxia is doubtful, and all the above types are classed as ideational apraxia. Kinetic apraxia is a defect at a lower level of performance and is traceable to the overaction of sensory factors in movement. It occurs in two general types: one related to frontal lesion and traceable to overaction of all positive contactual reactions, such as the grasp reflex; and the other related to parietal lobe lesions and related to overaction of withdrawal reactions, such as tactile avoiding. These disorders affect all movement and use of the limbs and also facial expression. Bilateral lesion affects gait most severely, but it also affects ability to stand or sit. Damage to the brain in infancy, when the integration of sensory factors in movement is not fully developed can result in exaggerated apraxia of these types in the absence of paralysis. The child's limbs either tend to flex on contact with a surface (repellent apraxia) or to extend too stiffly (magnetic apraxia). Damage to the basal ganglia results in unduly persistent forms of the same reactions, producing overextended or overflexed postures that are recognized as dystonia. Instability of integration at this level results in athetosis. The significance of these disorders of movement is discussed in relation to the usual concepts of pyramidal and extrapyramidal lesions. 59 references. 13 figures.—*Author's abstract.*

34. *Posthemiplegic Reflex Sympathetic Dystrophy.* EUGENE MOSKOWITZ, HAROLD F. BISHOP, HLA PE, AND KINICHI SHIBUTANI, Valhalla, N. Y. J.A.M.A. *167*:836–838, June 14, 1958.

The authors describe a painful syndrome in the affected upper extremity of 6 hemiplegic patients presenting the characteristics of a reflex sympathetic dystrophy. They did not respond to the usual rehabilitation procedures until ipsolateral stellate ganglion blocks were performed. The pain and other associated trophic changes were relieved, permitting more intensive physical therapy. In 2 patients, high thoracic sympathectomy was necessary to

afford more lasting benefit. Early recognition of the disability is important to prevent irreversible contractures of the fingers and to overcome the pain, permitting the patient to utilize whatever latent function may be present in the extremity. The skeletal changes, characterized by spotty demineralization in the bones of the hand, persist despite the clinical and functional improvement. 9 references. 4 figures.—*Author's abstract.*

35. *Neurologic Manifestations of Myxedema.* STEWART N. NICKEL AND BOY FRAME, Detroit, Mich. Neurology *8*:511–517, July, 1958.

The nervous system is significantly involved in myxedema, and a number of the major and initial manifestations are neurologic in origin. A review of the literature and a study of 100 patients with primary myxedema was made to determine the extent of neurologic dysfunction in this disease. Impairment of cerebrocortical function was manifested to some extent in all patients. The major focus of attention in the past has been devoted to organic mental changes ranging from anxiety to severe schizoid behavior. In this series, a 19 year old man presented the clinical picture of catatonic schizophrenia, whereas a 56 year old woman presented signs of intellectual deterioration and a paranoid personality thought initially to be Alzheimer's disease. Recently, interest has been aroused among clinicians, especially in England, in the occurrence of coma in severe cases of myxedema. Of these patients, 25 per cent developed grand mal convulsions preceding the comatose state. In this study, deep and fatal coma was noted to develop progressively from lethargy and irrational behavior in 1 patient over a period of seven hours. Defects in coordination are common in patients with myxedema. The gait has been observed to be unsteady, and the hand and tongue noted to be slow and clumsy. Manifestations of altered cranial nerve function included decreased visual acuity, diplopia, deafness, vertigo, tinnitus, depression of taste and smell, and facial neuralgia. A peripheral neuritis, primarily sensory in type, was noted to occur in myxedema in addition to the characteristic slow rebound of the deep tendon reflexes. The cerebrospinal fluid protein was tested in 8 patients and found to be elevated in all, reaching as high as 208 mg. per cent. Psychometric examination of 6 patients with myxedema showed definite mental deterioration in all. Mucinous involvement of the nervous tissue as well as vascular enzymatic abnormalities were suggested as possible mechanisms of action for the changes observed. 28 references. 2 tables.—*Author's abstract.*

36. *Cerebral Vasospasm—Clinical and Experimental Evidence.* J. LAWRENCE POOL, SHERWOOD JACOBSON, AND THOMAS M. FLETCHER, New York, N. Y. J.A.M.A. *167*:1599–1601, July 26, 1958.

Clinical and laboratory observations indicate that in animals and in man the larger arteries of the brain, such as those of the circle of Willis, are capable of vasospasm. The clinical significance of these observations is of particular importance with regard to the vasoconstriction occasionally seen on angiography or at surgery adjacent to an intracranial aneurysm that has recently bled. Experiments carried out in the anesthetized cat, dog, and monkey indicated that artificially imposed mechanical stimuli applied to the larger cerebral arteries resulted in promptly visible local vasoconstriction. The smaller arteries of the brain reacted with proportionally less vasoconstriction when subjected to similar mechanical

stimuli. Vasodilatation can be induced by topical application of 2 per cent procaine or 3 per cent papaverine after dissection to discover which stimuli have produced vasospasm. Of the two, papaverine has the greater effect. Neither was effective when given intravenously or intra-arterially. It is postulated that both a neurogenic and a local muscle response may play a role in the production and maintenance of cerebral vasospasm. These responses to trauma appear to be the same whether the stimuli are mechanical during an experiment or are the result of a disease process, such as rupture of an aneurysm. 8 references. 2 figures.—*Author's abstract.*

37. *The Prognosis of Some Brain Stem Vascular Syndromes.* ROBERT D. CURRIER, CONRAD L. GILES, AND MARTHA R. WESTERBERG, Ann Arbor, Mich. Neurology *8*:664–668, Sept., 1958.

A follow-up study was done on all patients with the clinical picture of thrombosis of the superior, anterior-inferior, or posterior-inferior cerebellar arteries seen at the University Hospital in the period 1934 to 1957. Seventy-five cases were found; 2 were of the anterior-inferior, 11 of the superior, and 62 of the posterior-inferior cerebellar arteries. All were followed up. Many were re-examined. Three-quarters of the patients were men. The average age was 56 years. Two-thirds had other evidences of vascular disease or diabetes. Thirty-eight of the 62 with posterior-inferior syndrome were dead: 15 from further cerebrovascular accident, 10 of coronary thrombosis, 4 of suicide, 9 from other causes. Of the 62, 46 per cent were dead five years after the onset, the survival time varying with the age and presence of other vascular disease. The superior cerebellar artery syndrome had a similar prognosis. If the posterior-inferior cerebellar artery syndrome is due to occlusion of the vertebral artery, then vertebral artery occlusion may have a survival time similar to that of all "strokes," a fact that should be considered when evaluating anticoagulant therapy. 23 references. 10 tables.—*Author's abstract.*

38. *The Diagnosis and Treatment of Wilson's Disease.* C. G. WARNOCK AND D. W. NEILL, Belfast, Ireland. Brain *81*:258–267, 1958.

Kinnier Wilson's classical thesis (1912) on hepatolenticular degeneration gave rise to all subsequent speculations upon liver-brain relationship, and, as a result, many such syndromes have come to light. Meanwhile Wilson's disease itself has become submerged in a morass of unrelated clinicopathological conceptions. This paper stresses the fact that hepatolenticular degeneration is a unique entity, not to be confused clinically, pathologically, or biochemically with any other type of hepatic encephalopathy. Three cases are described, all with metabolic abnormalities of the type nowadays accepted as typical of Wilson's disease, and with definite clinical resemblance to it. Only one, however, conforms to the essential diagnostic criteria. The authors regard corneal pigment (Kayser-Fleischer rings) as the only pathognomonic outward manifestation, without which clinical diagnosis can never be certain. Their cases showed biochemical abnormalities that might be accepted as diagnostic, if one believes that the biochemical picture is unmistakable. But laboratory and clinical diagnosis are equally misleading, in the absence of Kayser-Fleischer rings. It is emphasized that diagnosis in the preneurological phase can, and should, be established, and that treat-

ment should be started at this stage if there is to be any hope of lasting results. In the opinion of the authors, penicillamine (β, β-dimethylcysteine) is more valuable, and more practical for routine use, than any of the other therapeutic agents so far employed. 25 references. 2 figures. 1 table.—*Author's abstract.*

CEREBROSPINAL FLUID

39. *Technique to Avoid Spinal-Tap Headache.* ROBERT J. BROCKER, Pittsburgh, Pa. J.A.M.A. *168*:261–263, Sept. 20, 1958.

Specific precautions should be taken to avoid postpuncture cephalalgia, which is caused by leakage of cerebrospinal fluid. Therefore, any positioning or maneuvering that decreases the negative epidural pressure or decreases leakage should prevent postpuncture cephalalgia. Epidural negative pressure may be decreased by epidural venous distention through abdominal compression, and by hyperextension of the neural axis in which the dura in the lumbar area is forced up against the vertebral lamina. The hyperextension, in addition, staggers the dural and arachnoid vents and thereby makes leakage less likely. Small needles also decrease potential leakage by decreasing the size of the dural and arachnoid defects. The author performed 1094 punctures with a no. 18 spinal needle in the onside knee-chest position; 894 of the patients were advised to lie on the abdomen for three hours and 200 on the back for three hours before ambulation. In this test group of 894 patients, the postpuncture cephalalgia was less than 0.5 per cent, and in the control group of 200 patients the incidence was 36.5 per cent. The average incidence for all reviewed literature using no. 18 spinal needle was 41 per cent. Placing the patient on the abdomen decreased the incidence of headache by the mechanism described. The incidence should be even further decreased by using smaller needles. 1 reference. 1 figure.—*Author's abstract.*

CONVULSIVE DISORDERS

40. *Focal Seizures Due to Chronic Localized Encephalitis.* THEODORE RASMUSSEN, J. OLSZEWSKI, AND D. LLOYD-SMITH, Montreal, Quebec. Neurology *8*:435–445, June, 1958.

This is a report of 3 children with focal seizures apparently due to unsuspected chronic localized encephalitis. Histological examination of hemicorticectomy specimens in 2 of the patients and of autopsy material in the third suggests that an encephalitic process may smolder along for several years, causing focal seizures and gradually destroying areas of brain without showing clinical signs and symptoms that ordinarily lead one to suspect encephalitis. 11 references. 13 figures.—*Author's abstract.*

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

41. *Peripheral Neuropathy in Multiple Sclerosis.* JACK HASSON, R. D. TERRY, AND H. M. ZIMMERMAN, New York, N. Y. Neurology *8*:503–510, July, 1958.

Samples of peripheral nerves were examined in 20 necropsied cases of multiple sclerosis. In 6 cases, the median and ulnar nerves at the wrists and the posterior tibial nerves below

the knees were examined; widespread fascicular demyelination affecting nerve fibers over long distances was found in 5 of these, of which 4 had lesions of a severe degree. Only fragments of the major nerve plexuses were examined in 8 cases; demyelination was severe in 1 of these and moderate in 5. Portions of the femoral nerves only were examined in the 6 remaining cases; severe degeneration was demonstrable in 1, and the other 5 disclosed no evidence of myelin destruction. The pathologic changes were distinct from the plaque-like lesions of multiple sclerosis and consisted of a fascicular demyelination of nerve fibers over long distances associated with variable amounts of free and phagocytosed neutral fat. These alterations have frequently been observed in the course of avitaminosis and malnutrition. That all 5 cases with severe neuropathy were malnourished was apparent from the fact that all were emaciated and that 5 of them had decubiti. These ulcers are related to states of malnutrition. None of the cases showed evidence of diabetes mellitus, heavy metal intoxication, diphtheria, amyloidosis, or collogen disease. It is well known that in all types of peripheral neuropathy the distal portions of the nerves are affected most severely. It is noteworthy that the highest incidence and the severest degree of demyelination occurred in those cases in which multiple, distal peripheral nerves were examined. 10 references. 8 figures. 1 table.—*Author's abstract.*

42. *Relationship of Dystrophia Myotonica (Myotonic Dystrophy) and Myotonia Congenita (Thomsen's Disease).* J. E. CAUGHEY, Dunedin, New Zealand. Neurology *8*:469–475, June, 1958.

There is wide divergence of opinion as to the relationship, if any, of myotonia congenita and dystrophia myotonica. Originally dystrophia myotonica was regarded as a variant of myotonia congenita. Adie, Greenfield and others regard the two affections as being quite distinct, whereas Guillan, Rouques, Maas, and Paterson affirm that myotonia congenita is a variant of dystrophia myotonica. A family is described in which two brothers of the first generation had dystrophia myotonica. The son of one of these had myotonia congenita without other dystrophic features. This family appears to be an intermediate between the two types of myotonic dystrophy, with members representative of both dystrophia myotonica and myotonia congenita. It suggests a definite link between the two disorders. Given forms of dystrophy usually breed true, and most families with dystrophy have combinations of signs and symptoms peculiar to themselves. The generalization can be applied to the myotonic dystrophies. The family reported supports the suggestion that dystrophia myotonica and myotonia congenita are related disorders, and the relationship is probably due to one or all of the following factors: (1) Variable expressivity of the mutated gene, (2) differences in the genetic background upon which the mutation is operating, (3) variation in environment. 12 references. 4 figures.—*Author's abstract.*

43. *The Neuropathy of Multiple Myeloma.* MAURICE VICTOR, BETTY Q. BANKER, AND RAYMOND D. ADAMS, Boston, Mass. J. Neurol., Neurosurg. & Psychiat. *21*:73–88, May, 1958.

Multiple myeloma may be associated with a polyneuropathy that does not depend on compression of nervous structures by tumor tissue. The clinical findings in 5 such cases

are presented; in 3 of these, postmortem examinations were performed. The polyneuropathy, although varying in severity, took a characteristic form in 4 patients. Essentially, it was a symmetrical, atrophic, areflexic, sensorimotor affection of the legs, and in 2 cases of the arms. The fifth patient presented a mild sensory polyneuropathy. The cerebrospinal fluid protein level was raised in 4 patients. In 3 patients the symptoms of polyneuropathy preceded those of multiple myeloma and completely dominated the clinical picture. In 2 patients there was a prolonged remission of both the neuropathy and the myeloma. The neuropathy of multiple myeloma bears a close resemblance to that of carcinoma of the type unrelated to direct involvement by neoplasm. It is emphasized that in patients with obscure neuropathies, a careful search for both carcinoma and multiple myeloma should be made. Pathologically, there was no evidence of compression of neural structures by myeloma or by vertebral deformity. Microscopically, no plasma cells were seen in the nerves or roots. The most striking feature was the degeneration of the peripheral nerves and, to a lesser extent, of the anterior and posterior roots, always more in the distal segments than in the proximal ones. Both the myelin sheaths and the axis cylinders were destroyed, the former more than the latter. Relatively few dorsal root ganglion cells were lost. No amyloid was seen in the endoneurium or in the contiguous blood vessels. 46 references. 5 figures.—*Author's abstract.*

ELECTROENCEPHALOGRAPHY

44. *The Electroencephalogram During the Convulsive Seizure of Electroshock.* Y. PIETTE, Ostend, Belgium. Acta psychiat. et neurol. *58*:219–230, March, 1958.

The author has recorded electroencephalograms during the convulsive seizure produced by electroshock in man. One hundred milligrams of succinylcholine iodide were injected intravenously and produced a record free from artefacts. Spikes and sharp waves were more frequent in the temporal regions. In the centroparietal region, and most of all in the frontal regions, the record was slower and principally composed of waves of high voltage of ± 3 cycles/second, often having the appearance of spikes and waves. The bioelectric seizure suddenly ended with electric silence. Pre-electroshock injection of thiopental in the vein modifies the aspect of the record by reducing the frequency of the electric waves and the number of spikes and shortening the duration of the bioelectric seizure. Injection of thiopental does not diminish the efficacy of electroshock. These findings lead the author to conclude that the cortical bioelectric seizure of electroshock does not play an important part in the therapeutic mechanism. 8 references. 6 figures.—*Author's abstract.*

45. *Electroencephalographic Findings in Aged Psychiatric Patients.* WALTER D. OBRIST AND CHARLES E. HENRY, Durham, N. C. J. Nerv. & Ment. Dis. *126*:254–267, March, 1958.

Electroencephalograms were recorded on 103 psychiatric patients more than 65 years old. Comparisons were made between patients with chronic brain syndrome and those with functional disorders. A high incidence of diffuse slow activity (delta and theta) was found in the brain syndrome group. Functional cases, on the other hand, had a significantly greater number of normal tracings. Outcome of illness after one year was related to both

EEG findings and psychiatric diagnosis. Focal slowing occurred predominantly in the left anterior temporal region but was not related to psychiatric diagnosis. Cerebral vascular disease and congestive heart failure were consistently associated with EEG abnormalities. 24 references. 4 figures. 5 tables.—*Author's abstract.*

46. *The EEG as a Diagnostic and Prognostic Aid in the Differentiation of Organic Disorders in Patients over 60.* E. C. TURTON, Bristol, England. J. Ment. Sc. *104*:461–465, April, 1958.

The purpose of the investigation was to assess the value of the electroencephalogram (EEG) as an objective aid to the diagnosis and prognosis in elderly psychiatric patients. The increased number of these patients was pointed out. It was noted that there were two main categories: those suffering from an affective disorder, usually depressive, or those with an organic dementia, either arteriosclerotic or senile. Although the diagnosis is often clear cut, the point was made that there is a small mixed group that, at any rate initially, presents considerable diagnostic difficulties. All the elderly patients admitted to a psychiatric hospital over a 5 year period were examined, as far as possible. It was hoped that there would be a correlation between the degree of EEG change and the degree of dementia; however, although the EEG was usually abnormal in the more severe degrees of dementia, in the milder and doubtful cases clinical judgment was more satisfactory. Thus, although typical slow wave changes are often present in severe degrees of dementia, they are by no means always so and, in any case, these patients are not a clinical problem. In the mixed cases, where there may be both affective and organic components, the EEG does not appear to be a satisfactory diagnostic weapon for routine use, and ordinary clinical observation is more satisfactory. 8 references. 4 tables.—*Author's abstract.*

47. *The Effect of Meprobamate on the Electroencephalogram.* CHARLES E. HENRY AND WALTER D. OBRIST, Hartford, Conn. J. Nerv. & Ment. Dis. *126*:268–271, March, 1958.

Electroencephalograms were recorded on 100 psychiatric patients taking meprobamate orally. Rhythmic fast activity resembling that seen with barbiturates was observed in 85 per cent. Ten out of 12 patients given a single acute dose showed an increase in fast activity. 7 references. 2 figures. 4 tables.—*Author's abstract.*

HEAD INJURIES

48. *Practical Examples for Diagnosis and Treatment of Skull-Brain Injuries.* W. UMBACH, Freiburg, Germany. Medizinische *10*:1102–1105, Aug., 1957.

After injuries of skull and brain, long-lasting disturbances in vegetative regulation, circulation, and physical ability are frequently seen. Organic malfunctioning because of insufficient blood supply after irritation of the central vasoregulators is often diagnosed as psychogenic malfunction and compensation neurosis. The two following examples show how important it is to proceed with an exact evaluation in order to diagnose the cerebral and circulatory damage. The first case concerned a penetrating injury of the left frontal lobe which was treated and covered by plastic surgery. There was a progressive pseudo-

neurasthenic malfunctioning. Tentative diagnosis was symptomatic psychosis. Only after pneumoencephalography and arteriography (which was never done before) was a big cavity in the left frontal lobe with communication into the ventricle to be seen. After surgical connection with the cortex, the patient showed slow improvement. In the second case it was assumed that the cause of the severe circulatory disturbance was malingering and compensation neurosis, whereas circulatory tests showed that a severe disturbance of the diencephalic regulators had resulted from the accident.—*Author's abstract.*

INFECTIOUS AND TOXIC DISEASES OF THE NERVOUS SYSTEM

49. *Neurological Disorders Associated with Asian Influenza.* BRIAN MC CONKEY AND R. ALEX DAWS, Cardiff, Wales. Lancet 2:15–17, July 5, 1958.

Four patients developed neurological disorders three days after a short febrile illness that was shown, by complement fixation tests, to be Asian influenza. Antibodies were present in the blood at titers of 1:64 to 1:2408 for influenza A; and by hemagglutination inhibition at titers of 1:32 to 1:512 for the Asian variety. Two patients were brother and sister; all of their family had significant titers for influenza A (Asian), one of them also having a similar neurological illness. Three of the patients described had encephalitis with typical electroencephalographic appearances. One of them when acutely ill showed improvement following the administration of cortisone and penicillin. The remaining patient had an illness resembling lymphocytic choriomeningitis; the results of her serological tests were not so clear-cut as the others. All of them appeared to make complete recoveries. 6 references. 3 figures.—*Author's abstract.*

50. *Acute Cerebellar Syndrome of Childhood.* MICHAEL E. BLAW AND JOHN C. SHEEHAN, Ann Arbor, Mich. Neurology 8:538–542, July, 1958.

Acute cerebellar ataxia in childhood has been observed as a complication of various etiologically defined infectious diseases and, as reported in this paper, following nonspecific upper respiratory infections. The disease occurs in children less than 4 years of age. There is a well-defined latent period between the upper respiratory illness and the onset of cerebellar symptoms. The disease is acute in onset and nonfatal. Truncal ataxia is a constant finding, although upper extremity tremor and nystagmus are seen with some regularity. Residual neurological deficits are not common. The clinical course suggests a viral etiology. 11 references. 1 table.—*Author's abstract.*

INTRACRANIAL TUMORS

51. *The Meningiomas of the Lateral Ventricles of the Brain.* S. ANTHONY TUKANOWICZ AND FRANCIS C. GRANT, Phila., Pa. J. Neuropath. & Exper. Neurol. *17*:367–381, April, 1958.

A series of 8 cases of meningiomas of the lateral ventricle of the brain is presented out of a total of 407 intracranial meningiomas selected from the tumor registry of the Hospital of the University of Pennsylvania. Seven cases were histologically verified as fibroblastic

meningiomas. The eighth case was found to be meningoendotheliomatous in type. A tumor of this type and in this location has not been reported previously. There was 1 postoperative death giving a postoperative mortality of 12.5 per cent. In the remaining 7 patients survival time varied from 6 months to 14 years. One patient lived for six months, 1 for seven months, 1 for 22 months, and a fourth patient died of epidural abscess 16 months after the primary operation. In the 3 living patients there is no evidence of recurrence of the tumor. The longest survival period is 14 years. The second patient is alive 12 years and the third four years after the operation. A survey has been made of the clinical signs and symptoms in all cases. The most common signs and symptoms are headache, nausea, vomiting, papilledema, visual disturbances, and disturbances of motility and sensitivity. No definite clinical syndrome has been defined by which these tumors may be diagnosed. The most precise method of diagnosis is ventriculography. Ventricular estimation may also be helpful in reaching a diagnosis. All tumors were encapsulated; therefore all were completely curable if removed in their entirety. The operative approach is either by transcortical incision in the nonvital area or by removing an area of the cortex overlying the tumor. 14 references. 8 figures. 1 table.—*Author's abstract.*

TREATMENT

52. *Clinical Evaluation of Spirodon.* GILBERT FRANK AND FRANK MORRELL, Minneapolis, Minn. Neurology 8:529–537, July, 1958.

Twenty-nine seizure patients with long histories of poor control on large doses of anticonvulsants were recently given a new spirohydantoin compound (Spirodon), for periods of from 1 to 18 months. Fifteen patients (52 per cent) were significantly improved (*t* test, $t = 2.58$). Consideration of patients according to clinical seizure type indicates that Spirodon has most promising action in patients with psychomotor seizures; 10 of 16 cases (62.5 per cent) with psychomotor seizures were improved. Electroencephalographic correlation showed that 5 of 7 patients (71.5 per cent) with isolated focal lesions (6 of these were temporal lobe foci) were improved while taking Spirodon. Toxic reactions consisting chiefly of rash, lethargy, psychomotor retardation, ataxia, and confusion occurred in 17 patients (59 per cent); however, only 9 (32 per cent) of these needed to have the drug withdrawn. One patient developed significant leukopenia (1900 white blood cells/cu. mm.) All toxic reactions cleared rapidly after withdrawal, and no serious aftereffects were noted. The effective dose averaged 2 Gm./day; the toxic dose averaged 2.5 Gm./day. The maximum dose used in this study was 4 Gm./day. Spirodon deserves further trial on a larger series of patients, because it shows promise in controlling a large and very difficult group of seizures. Toxic reactions are not uncommon but are usually quite obvious and readily reversed by withdrawal. 3 references. 4 tables.—*Author's abstract.*

53. *Thirty Years of Progress in Therapy for Paralysis Agitans (Parkinson's Disease).* LEWIS J. DOSHAY, New York, N. Y. J.A.M.A. *167*:1195–1197, July 5, 1958.

From small beginnings in the third decade of this century, an impressive armamentarium has evolved for the treatment of paralysis agitans (Parkinson's disease), along with a clearer

understanding of the nature and management of the disease. The Spanish influenza epidemic of 1918 resulted in so many cases of epidemic encephalitis (lethargic encephalitis) that feverish efforts throughout the world were concentrated on discovering a vaccine that would prevent this terrible disease and its sequelae of Parkinsonian symptoms. These efforts failed, and by 1928 the aim was to find measures that would effectively combat the symptoms. Overenthusiastic claims were made at first for various belladonna preparations, but with time and further observation these proved disappointing. Neurosurgery was explored next. Every segment of the brain, spinal cord, and nerve roots was severed, but, in the absence of knowledge as to the areas and pathways responsible for tremor and rigidity, these surgical efforts were destined to failure and were abandoned by 1945. The 1950's witnessed a resurgence of medicinal remedies, spearheaded by synthetic compounds, to replace the solanaceous drugs, which not only had disturbing side reactions but also were unsuited to older patients because of the hazard of glaucoma. Also, within the past five years active interest in neurosurgery has been revived, with the attack now concentrated entirely on the basal ganglia, especially the globus pallidus. Finally, within the past year the Parkinson's Disease Foundation has come into existence, with its goal of research into the cause and prevention of the disease. Thus the outlook for patients with Parkinson's disease is much brighter than it was 30 years ago. 9 references.—*Author's abstract.*

54. *Long-Range Effects of Electropallidoansotomy in Extrapyramidal and Convulsive Disorders.* E. A. SPIEGEL, H. T. WYCIS, AND H. W. BAIRD, III, Philadelphia, Pa. Neurology *8*:734–740, Oct., 1958.

Of 49 cases with tremor unresponsive to medication, 22 (44.9 per cent) showed a marked reduction or abolition of tremor and 16 (32.6 per cent) showed a moderate tremor reduction, with a total improvement of 77.5 per cent. Rigidity was definitely reduced in 26 (72.2 per cent) of 36 patients so affected prior to surgery. A complete rehabilitation, enabling the patients to resume their former occupations, was obtained in 9 of 50 patients (18 per cent), and partial rehabilitation resulted in 15 (30 per cent). In certain types of choreas (Huntington chorea) and in some instances of athetosis and torsion dystonia improvement could also be obtained. In this group, production of transitory depression of pallidal function by procaine injection helps one to select the proper cases for production of permanent lesions. Pallidal lesions are able to diminish the tonus of the skeletal muscles in some cases of spastic paralysis where the existence of increased tendon reflexes and the Babinski phenomenon suggests an involvement of the corticospinal tract. The effect of pallidoansotomy alone or combined with amygdalotomy was studied in a group of epileptic patients in whom seizure discharges were demonstrable in these ganglia and in whom anticonvulsive medication was ineffective. The seizures were controlled or their frequency markedly diminished in 7 of 12 cases (58.3 per cent) despite a drastic reduction of the medication. Of 8 cases with salaam seizures, 6 were improved. 24 references. 1 figure. 7 tables.—*Author's abstract.*

55. *An Evaluation of Thymectomy in Myasthenia Gravis.* JOHN A. SIMPSON, London, England. Brain *81*:112–144, March, 1958.

This paper analyzes the London experience of thymectomy, the largest series and longest

follow-up available. The operated series (258 without tumor, 36 with thymoma) is compared with an unselected series of medically treated cases of myasthenia (99 without tumor, 11 with thymoma). Analysis of various factors in the history showed that the series were comparable. It is concluded that significantly fewer die of myasthenia gravis (nontumor) if their thymus is removed than would be expected if they were treated with neostigmine only, and the number of women very greatly improved 10 or more years after the onset of the illness is significantly greater. The improvement is most evident, and the saving in life is greatest, when the duration of the disease is less than five years and when it occurs in women under 30 years of age, but it is not confined to this group. After seven years from the onset, considerable improvement after operation is less likely but may still occur. However, the risk of death from myasthenia is then less whether operated or not. Similar improvement occurs in men but to a lesser extent. The prognosis for life remains poor if a thymoma is present, but preoperative radiotherapy may be beneficial. Only 1 patient in 3 survives, but the improvement in myasthenia may then be as great as in nontumor cases. No indications for case selection were found. Purely ocular myasthenia is best treated conservatively, but if generalization occurs early operation is indicated. The neostigmine requirement before operation is no guide to the ultimate postoperative status. The results are compared with American series, and the apparent disagreements are shown to be due to: (1) Failure to analyze tumor cases separately, and (2) methods of selection. 27 references. 2 figures. 25 tables.—*Author's abstract.*

BOOK REVIEWS

The Criminal Mind. PHILIP Q. ROCHE. New York. Farrar, Straus and Cudahy, 1958. 299 pp. $5.00.

This volume, an expansion of the fifth series of Isaac Ray Lectures, presented by the author at the University of Michigan in 1957, bears the subtitle "A Study of Communication Between the Criminal Law and Psychiatry." The author has had a long experience in the field of forensic psychiatry, both in its applications to the court and to the correctional institution, and his writings led to his selection as "most worthy by reason of his contribution to the improvement of the relations of law and psychiatry," to use the wording of the award made annually by the American Psychiatric Association. His basic thesis is that what the psychiatrist and the lawyer choose to consider the "real world" is colored by language habits, and that "the verbal world of abstraction is illusory and detached from the facts of life." Thus true reality consists not so much in how we define such terms as "mental illness" as in what we do to people whom we label with that term. The fact that the lawyer's model of action is public centered and authoritative, whereas that of the psychiatrist is individual centered and susceptible to reassessment and alteration, makes communication difficult and inherently disposed to tension. As illustrations of his thesis, he cites cases in the pretrial, trial, and post-trial phases. To the psychiatrist, some of those cases are shocking indeed, that is, if he is not aware of the almost savage strictness of interpretation of psychiatric data exhibited from time to time by the courts of Pennsylvania.

In the concluding chapter the author considers the Durham rule. He favors the rule, as do most students of the problem of the so-called tests, since it permits the psychiatrist to

become a reporter of observations instead of a "moral inquisitor." He recommends as a procedural modification that the psychiatrist report objective data, but that the question of product be left to the triers and not asked of the expert. This would, he says, "complete the work of liberating medical testimony from the ghost of M'Naghten." Finally, as a long-range goal, he urges the establishment of a treatment tribunal rather than the determination in the trial of the defendant's mental state and the disposition that will best protect society. The volume is a valuable addition to the growing literature on forensic psychiatry.—*Winfred Overholser, M.D.*

Child Psychiatry, ed. 3. LEO KANNER. Springfield, Ill. Charles C Thomas, 1957. 777 pp. $8.50.

This new edition of a universally accepted text fulfills splendidly the task the author set for himself in 1930: ". . . to teach pediatricians how to handle the rank and file of children's personality disorders, which they usually would not and, if properly trained, should not refer to a psychiatrist." A large section of the book discusses personality development, family relationships, and the child's environment. Later sections deal with specific symptoms and syndromes, placing particular stress on the organic substrates in many psychological difficulties. It is to the author's great credit that he overemphasizes neither the organic nor the psychological, and that he observes a melioristic view throughout. Studded with excellent clinical descriptions and numerous short case histories, the writing is notable for its clarity, simplicity, and pragmatic thinking. Though not written within a psychoanalytic framework, much of the psychotherapeutic material is nonanalytic in wording only. There are a number of references to the significance of unconscious motivation, and the importance of understanding the relationship between doctor and child is repeatedly stressed and explained in clinical synopses. The author makes the psychotherapeutic process understandable, thereby greatly increasing the number of children who can be helped in a sound way. Because of the publication date, there is no discussion of the impact of ataractic drugs on pediatric treatment. This is a splendid book for teaching medical students and for the pediatrician's immediate reference library.—*Sidney L. Werkman, M.D.*

Psychopathology of Communication. Edited by PAUL H. HOCH AND JOSEPH ZUBIN. New York. Grune & Stratton, 1958. 310 pp. $6.75.

Sixteen papers presented at the 1956 annual meeting of the American Psychopathological Association, discussions of 11 of these papers, and Oskar Diethelm's presidential address constitute this book. Five papers are concerned with communicative problems of children. One study deals with problems of conceptualization and communication in children with developmental alexia, one with autistic patterns in blind children with retrolental fibroplasia, and one with the reactions of schizophrenic children to delayed auditory feedback. The tangential response is analyzed, and its influence on personality development is discussed. Waiting room observation is shown to be a useful technique for analysis of communicative behavior in children and their parents Changes in language patterns are analyzed as seen during electroshock therapy and as an adaptive mechanism in organic brain disease. Five reports deal with various aspects of communication in psychotherapy.

Investigation of the communicative process may become so involved in the process of recording and the ingenious use of various electronic gadgets that the reported results come as an anticlimax following the presentation of the method of study. Few papers in the symposium show this weakness. The book is, on the whole, well worth reading. There is, however, little to warrant the editors' statement in the foreword that "long neglected by social scientists, maligned as unreliable and invalid, the interview can now be brought into the storehouse of scientific tools and sharpened until it can cut effectively into the unsolved problems of mental disease."—*Margaret Mercer, Ph.D.*

The Slow Learner. Some Educational Principles and Policies. M. F. CLEUGH. New York. Philosophical Library, 1957. 186 pp. $3.75.

The author discusses the provisions for mentally handicapped children in England with special reference to British legislation for educationally subnormal pupils. The Education Act of 1944 replaces the concept of "mental deficiency" by the broader concept of "educational subnormality" and provides a specialized form of education for the children affected. The act has resulted in a great expansion of new services, such as schemes for special educational treatment in regular schools, new special schools, and remedial centers. The author seems well equipped to report and comment on these new educational principles and policies because she has been in charge of the Diploma Course for teachers of subnormal children at the University of London Institute of Education. However, any publication dealing with policies has the limitations of the time in which it is written. Thus, new legislation had already superseded that under scrutiny in this book by the time it was in press. It seems, therefore, that the proper place for the material would have been a journal. Much of the need for change in school services is due to psychological discoveries and has its counterpart in this country. Although the educator will be interested in studying how the problem of the slow learner has been handled in England and will be stimulated by the author's astute observations and suggestions, the circle of other interested readers will probably be small. One wonders why the book appeared on the American market.—*Mirjam Mueller-Zbylut, Ph.D.*

Panic and Morale. IAGO GOLDSTON, editor. New York. International Universities Press, 1958. 340 pp. $5.00.

This book is based on the recorded proceedings of a conference on the nature of morale, held in 1954 under the joint auspices of the New York Academy of Medicine and the Josiah Macy, Jr., Foundation, with additional contributions from a previous conference on panic and morale under the same sponsorship. The participants were from the fields of medicine, psychiatry, psychoanalysis, social psychology, cultural anthropology, ethnography, sociology, economics, and political science. One paper, by George A. Miller of the Psycho-Acoustic Laboratory at Harvard University, discussed the elementary concepts of information theory. Succeeding papers dealt with radio and press communication in relation to morale and panic; the meaning, nature, and sociology of morale; causes contributing to panic and reactions to danger and catastrophe; and the role of various agencies and community resources in promoting morale and preventing panic. As is inevitable in such con-

ferences, the quality of the papers is variable, considerable time is given to semantic struggles, and many participants obviously find it difficult to communicate with people outside their own professions. However, the book is informative and thought-provoking, and there is an excellent bibliography. It can be recommended to those who want an over-all view of the problems of morale.—*Margaret Mercer, Ph.D.*

Integrating the Approaches to Mental Disease. Edited by H. D. KRUSE. New York. Paul Hoeber, 1957. 409 pp. $10.00.

This volume presents the proceedings of two conferences held under the auspices of the Committee on Public Health of the New York Academy of Medicine, conferences in which 48 eminent psychiatrists, psychologists, neurologists, and other students of human behavior participated. To review in any detail a volume of nearly 400 two column pages is nearly as impossible as to abstract *Who's Who in America.* The simile is apt for another reason than bulk, for the roster of participants is almost literally a who's who in Psychiatry.

In general, four schools of thought as to the causality of mental disorder were represented, namely, the organic, the experimental psychological, the psychodynamic, and the psychosocial. There seemed to be agreement, as we might expect except from the most extreme, that, as Alexander put it, "We deal with three, not opposing etiological theories, but complementary approaches to the total problem." Dunham, speaking for the psychosocial viewpoint, expressed his position: "Each theoretical position which we have considered has a too narrow range for encompassing a valid scientific explanation for the great variety of mental and behavioristic disorders." He adds that each position will have "significance with reference to certain categories of these disorders when we know what these categories are." Finally, he warns against revising any position when its hypotheses cannot be supported by available evidence. Most of the chapters consist of prepared papers, but several are made up of fairly free give-and-take discussion, well-edited and as clear and readable as any such arrangement can well be. Some of the general headings are Areas of Interdoctrinal Unacceptance, Evidence of Interrelations among Doctrines, Clinical Principles in the Practice of Psychiatry, Cross Criticism among Disciplines, and the Role of the Basic Scientist in Multidisciplinary Research.

Binger, in the closing discussion, says: "Until psychiatrists take the responsibility for defining the problems, planning the research, and then seeking assistance from experts in other disciplines as needed, I do not believe that research on mental disorders will make much headway. I doubt very much whether collaborate research is possible unless there is leadership. That is the psychiatrists' job. One of the reasons why we seem to be at cross purposes is that the psychiatrists themselves have not assumed this job." All psychiatrists would profit by reading this book and pondering it well.—*Winfred Overholser, M.D.*

The Epileptic Seizure. COSIMO A. MARSAN AND BRUCE L. ROLSTON. Springfield, Ill. Charles C Thomas, 1957. 251 pp. $6.00.

The inadequacies of conventional methods of diagnosis and localization of epileptic foci are pointed out particularly in psychic, visual, visceral, auditory, and other forms of focal epilepsy. The authors find that the history of the aura does not always reflect the true

focus. By reproducing an attack with intravenous pentylenetetrazol, they observe the pattern of the seizure, obtain data to supplement the other information, and are able to make clinical and electroencephalographic correlations. The pathogenesis of epilepsy is thus elucidated, and patterns of propagation of the epileptic discharge can be documented. The pattern and sequence of the pentylenetetrazol-induced attack are usually identical with those of a spontaneous attack, but the former permits controlled observation of patient and more valid inferences regarding the true site of the lesion. This is a valuable contribution to the clinical and investigative aspects of epilepsy, and consequently is of interest to the neurologist, surgeon, and research scientist.—*Harold Stevens, M.D.*

Sex Perversions and Sex Crimes. JAMES M. REINHARDT. Springfield, Ill. Charles C Thomas, 1958. 340 pp. $5.75.

The fact that this volume is a monograph in the Police Science Series and written by a professor of criminology should put the psychiatrist on guard. Far from being a "psychocultural study," as the dust jacket tells us, it is a recounting of cases of sexual perversion with comments largely of the "conditioned reflex" basis of behavior of this sort. There are frequent references to such authorities (?) as Salter and de River, but none to Karpman and only passing reference (in a slurring way) to the basic Freudian psychology or to such volumes as those by Caprio. There are frequent uses of such words as "degenerate" and "sex lust." The author says: "It would be very helpful to criminologists if in all serious sex criminal cases an investigation were also made by persons possessing some special qualifications for the study of the underlying motives." This is a sound aim. Unfortunately, very few inklings as to the "underlying motives" will be found in this volume.—*Winfred Overholser, M.D.*

The Education of Young Children. D. E. M. GARDNER. New York. Philosophical Library, 1957. 118 pp. $2.75.

This is a book about children of nursery school age written by a woman who not only knows and understands children but who loves them as well. The author's main purpose seems to be increasing the sensitivity of nursery school teachers to the needs of children. She writes, however, with such simplicity, charm, and clarity that the book should have immediate appeal to a much wider audience. Parents would be less puzzled by their children if they had access to the book, and professionals would find it a light and delightful refresher in child psychology. Although the age of the sputniks has made the philosophy of the whole child unpopular, the reader can only be impressed with it all over again as it is applied to this particular age group. The author describes the feelings of these moppets and the nature of their interaction with each other wonderfully well. She reviews concisely but thoroughly the way a child thinks and learns, and makes cogent suggestions on ways in which the adult may intervene with constructive results. She includes the prerequisites and preparation for nursery teaching since she feels that the nursery school of the future will play an important role in the development of sound mental health. A full bibliography and some excellent plans are provided.—*Robert Konrad Kahn, Ph.D.*

An Introduction to Psychopathology. D. RUSSELL DAVIS. London, England. Oxford University Press, 1957. 388 pp. $7.50.

Administrative Medicine—Transactions of the Fifth (1956) Conference. GEORGE S. STEVENSON, editor. New York. Josiah Macy, Jr., Foundation, 1958. 197 pp. $3.75.

Ego Psychology and the Problem of Adaptation. HEINZ HARTMANN, translated by DAVID RAPAPORT. New York. International Universities Press, 1958. 121 pp. $3.00.

Existentialism and Education. GEORGE F. KUELLER. New York. Philosophical Library, 1958. 169 pp. $3.75.

Epilepsy. MANFRED SAKEL, with preface by OTTO POETZL. New York. Philosophical Library, 1958. 204 pp. $5.00.

The Female Offender. CAESAR LOMBROSO. New York. Philosophical Library, 1958. 313 pp. $4.75.

Perceptual Process and Mental Illness. H. J. EYSENCK, G. W. GRANGER, AND J. C. BRENZELMAN. New York. Basic Books, 1957. 144 pp. $3.75.